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CHEMICAL DEVELOPMENTS AND OUR DAILY LIFE

THE celebration next week of the centenary of the Chemical Society (see *Nature*, July 5, p. 6), and the meeting of the International Congress of Pure and Applied Chemistry following it, afford a fitting opportunity to cast a glance at some of the more important applications of the science as they affect the daily life of the ordinary citizen. Despite progress in education, the great majority of people seem to have but an inkling of the part played by chemistry and its sister sciences in improving the material conditions of their existence, and very few have any real interest in the subject ; they will grasp for an aspirin, grab for a 'nylon' stocking or a coat of many colours, they make full use of the modern rapid means of communication, and relish the margarine that now masquerades as butter, without a thought that these innovations are the outcome of long and patient research in chemistry, physics or biology. One may excuse such ignorance and apathy in those who were born in Victorian days, but there is less excuse for the younger generations, although these also have been handicapped at school in their range of interests by too much concentration on the distant past.

For a few years following the First World War, Sir William Pope and others complained of the lack of recognition and recompense meted out to chemists, who were enjoined to become more vocal. Such complaint was well justified, but the suggested remedy, self-assertion, cannot be regarded as good professional etiquette. Though chemists have achieved marvellous discoveries in the last four or five decades, most of them realize that but for the co-operation of physicists, biologists and engineers, many of their discoveries would never have come to fruition. Almost everywhere we see the old rigid boundary lines between what Comte called the positive sciences breaking down, and it may be that before very long they will disappear completely, and by so doing lead to a better integrated outlook on the physical universe as a whole.

Of all the ramifications of chemistry in daily life—and their name is legion—the most significant have been made in engineering, food and agriculture, medicine and pharmacy ; but wherever we look we find that analytical chemistry is an indispensable aid in the control of production, from the raw material to the finished article.

Progress in metallurgy—the offspring of chemistry and physics and the fairy godmother of engineering—has been a determining factor in the evolution of this mechanical age. Within the last few decades methods of extracting from their ores metals like aluminium, nickel, chromium, tungsten and beryllium (also magnesium from sea-water) and improvements in the smelting of the older metals, together with the discovery of a multitude of new alloys, have added to the amenities of everyday life and markedly increased its *tempo*. Among the amenities may be mentioned unstainable cutlery, cooking utensils, nickel- and chromium-plated ware, metallic containers, electric-

lamp filaments, and various components of radio apparatus; and among the 'accelerators' that come to mind are bicycles and motor vehicles, turbines, speedier locomotives and improved railway lines, and modern aircraft.

From the bronze age down to the modern age of light alloys, civilization has advanced almost *pari passu* with the number of new materials available to man. These materials are either metals or non-metals, and both have contributed to the progress of agriculture, the former by providing better machines and the latter chiefly by providing fertilizers. Apart from Chilean nitrate and muriate of potash, all the common inorganic fertilizers—superphosphate, ammonium sulphate, basic slag, cyanamide, nitrate of lime and 'nitro-chalk'—are the products of chemical enterprise. They have enormously increased food supplies and have been of special importance during the recent years of austerity. It is true they have their denigrators, but the fact that the annual world consumption of them before the War approached 50 million tons should dispel any illusion that fertilizers are fooling all the farmers all the time. But scientific agriculture is by no means a preserve of chemistry, as Davy and Liebig believed. During this century, physics, botany and plant physiology, bacteriology, mycology, geology and even mathematical statistics have invaded the field and deprived her of her hegemony.

Chemical and biochemical research has provided new and very important knowledge of food values, and so given everyone the means of improving their diet and their health, would they only discard the myths and mumpsimus of a bygone age and learn what science has to teach. The discovery of the vitamins and enzymes and of the importance of certain minerals in the metabolism of man and farm livestock, and research on the proteins, are the outstanding achievements of the last few decades, while the very recent work on plant viruses, insecticides and phytocides has opened up vistas of healthier crops and increased production. Analytical chemistry has been, and still is, the custodian of purity and nutritive value in plant, animal and human food.

During the past century we have travelled far from the injunction of Paracelsus that "the object of chemistry is not to make gold, but to make medicines"; nevertheless the number of drugs and medicaments steadily increases. Phenacetin, antipyrine, lithium salts and salicylates have been succeeded, but not ousted, by aspirin and the narcotics, barbiturates and paraldehyde. Medicinal alkaloids and some hormones have been synthesized, glycero-phosphates introduced, and last but not least, the use of 'Mepacrin' and 'Paludrin' against malaria, and of sulphonamides and penicillin as antibiotics, bid fair to eliminate some of the worst diseases of mankind. Nor must one forget the value of anæsthetics and of many indispensable antiseptics like phenol, cresol, hydrogen peroxide, chlorine and hypochlorites. The discovery of salvarsan by Ehrlich in 1910 was a landmark in the history of curative medicine, as also was that of insulin by Banting and Best in 1921; and medicine aided by chemistry has reduced to relative insignificance such former scourges as plague, cholera, leprosy and dysentery. The end is not yet, for medico-chemical research workers are still imbued with the spirit of Louis Pasteur, as expressed in his favourite maxim, "Il ne faut pas s'arrêter aux choses acquises".

Engineering, and its offshoot chemical engineering, have been of the greatest service to the community in translating the results of chemical research into large-scale practice. The manufacture of soda by the Solvay process, of sulphuric and nitric acids and ammonia by catalytic processes, 'oil from coal' and the catalytic hydrogenation of vegetable oils, have been outstanding achievements in this connexion. In the recent great developments in the petroleum industry, the chemist and engineer have improved the refining of crude oil, and by 'cracking' this oil and the natural gas from oil-fields, have produced a large number of valuable chemicals, such as aviation petrol, synthetic rubber, and many kinds of solvents.

The chemist has also improved, or discovered, paints, varnishes, detergents and water-softeners, photographic materials, optical glass, explosives, tanning materials and artificial leather, and the bleaching, dyeing, printing and finishing of textiles. But perhaps the most spectacular achievement due essentially to the chemist has been the discovery of the artificial 'silks', Chardonnet, viscose, acetate 'silk', and the incomparable nylon. These, together with new and faster dyes, have not only increased the range of fabrics, but also added a welcome touch of colour to the somewhat sombre garments of our immediate ancestors.

The above sketch, necessarily incomplete, of the main achievements of applied chemistry during the last hundred years may well prompt the question as to the nature of the benefits they have conferred. The answer can only be that they are almost, if not quite, exclusively material benefits. Physical health as a foundation of mental health has improved, especially among people living in large towns, but otherwise the achievements have added only to the amenities—the conveniences, comforts and enjoyments—of life. The trouble is, as Goethe said, that "mankind progresses, but man remains the same". Not even the most enthusiastic of chemists can envisage the discovery of an alkahest that will dissolve all the long-chain compound troubles and disabilities of man that derive mainly from his animal ancestry, and so make him master of himself as well as of his surroundings.

SOVIET PHILOSOPHY

Soviet Philosophy

A Study of Theory and Practice. By Dr. John Somerville. Pp. xv + 269. (New York: Philosophical Library, Inc., 1946.) 3.75 dollars.

THIS is an interesting book. The most interesting section of it is to be found in the second part, and especially in Chapters 7 and 8, where an account is given of the development in Russia of the doctrine of dialectical materialism that enables one to see how alive philosophical discussion is in the U.S.S.R. and

how one development follows another. To read it is like reading an account of the history of the first Councils of the Christian Church, to follow the rise of one heresy after another and to see the truth decided by the decision of the Council after discussion.

According to Dr. Somerville, dialectical materialism was first given a thoroughgoing mechanistic interpretation; that was then routed by a Hegelian interpretation and condemned. The victor was in turn rejected, his doctrine described as a Menshevistic idealism and succeeded by the emphasis on social realism.

The first part of the book is disappointing. It begins with a fairly ordinary account of Marxian theory, and follows with what is very difficult to regard as anything but a silly discussion on the nature of democracy. Dr. Somerville is always putting up the most elementary and foolish misunderstandings of the views of Marx and Lenin and knocking them over with great ease. What impressed me most in reading this part of the book is how much Bolshevik argument depends on the use of a bogey called bourgeois capitalism. The bogey, as Bolsheviks and Dr. Somerville describe it, seems to me to have no resemblance to any industrial system in existence, even to that of the United States. Russia has been for so long shut up in the world that the Russians cannot be expected to know what contemporary civilization is like, and they obviously look at it entirely through the eyes of Karl Marx, who had a penetrating eye on the capitalism of a hundred years ago. If Dr. Somerville had regarded his own civilization with anything like the same amount of sympathy as he bestows on the Soviet Union, he would have written a much more illuminating book.

Dr. Somerville quite rightly says that you cannot interpret a living philosophy without getting inside it, and that you cannot do that without sympathizing with it, and he does not deny "a certain amount of sympathy". That statement is what is called a meiosis. Dr. Somerville seems to have abandoned criticism when he is confronted with Bolshevik theories; but it ought to be possible to have a sympathetic understanding of a system, as of a person, and yet recognize defects. After all, every political system has the defects of its qualities, and writers on the Soviet Union who portray it as if it were an exception to that rule do not help their cause.

Let me take an instance of Dr. Somerville's attitude. He starts with the ordinary exposition of the class war, a doctrine which starts with the recognition of classes, and then says that the antagonism of classes depends on the ownership of the means of production. That is simple and familiar. When he is confronted with the obvious fact that there are classes in the Soviet Union, in the sense of social divisions, he replies: "Oh, but those are not classes by Soviet definition, because by Soviet definition classes depend on ownership". By this ingenious sophistication he avoids facing the uncomfortable fact that divisions of social sympathy and misunderstanding are obviously arising in the Soviet Union; for example, one of the obvious developments of industry is that ownership is getting much less important, and the division between those who manage and those who are managed is the fundamental division of a modern industrial society. To run away from that fact by that kind of sophistication is surely childish.

LINDSAY OF BIRKER

AMERICAN PHILOSOPHY

(1) A History of American Philosophy
By Herbert W. Schneider. Pp. xiv+646. (New York: Columbia University Press; London: Oxford University Press, 1946.) 25*s*. 6*d*. net.

(2) American Philosophic Addresses, 1700–1900
Edited by Joseph L. Blau. Pp. xii+762. (New York: Columbia University Press; London: Oxford University Press, 1946.) 38*s*. net.

THE first of these books is a very thorough, well-arranged, well-documented piece of work, which is likely to be the standard text on its subject for a long time to come. Prof. Schneider begins with the Colonial period, when American philosophy was mainly theology inspired by Puritanism and, later, political theory inspired by Locke and the French eighteenth-century thinkers. He does not attempt to take his history as far as the present younger generation, but deals fully with that earlier generation, of whom two are still alive: the generation of Pierce, James, Royce, Santayana, Dewey, and one or two others less well known. With these thinkers there began new movements, still influential, characteristically American and having for the first time repercussions outside the United States. Santayana is properly included as American, because, however European by birth and later residence, he was influenced in his formative years by the environment of Boston and Harvard. That he reacted against the environment more than with it does not alter the fact that it was his environment. On the same grounds, Whitehead should not be claimed as American in spite of his having written his most important books there.

The second book is a useful companion volume, containing a number of characteristic statements by leading American thinkers, mostly of the earlier period. Some of these are interesting historical documents, which were not at all accessible until reprinted here. The necessary biographical information about the authors is given in brief.

In Britain we are still inclined to think of the philosophy of the United States as no more than an offshoot of European and mainly of British philosophy, if only because it is written in the English language. That was true enough a hundred years ago. Until then, as Prof. Schneider says, there was a brisk importation of ideas from Europe, and although they were reproduced with a distinctive American flavour, it was not much more than reproduction. In the second half of the nineteenth century a definite change came about. American thought developed on its own lines and is now a force to be reckoned with. One may object to the philosophy of John Dewey (as does Lord Russell, whose comments in his "History of Western Philosophy" are very severe); but that objection is evidence of its importance, as both representing and influencing modern life and thought. James Burnham, in his "Managerial Revolution", argues that the world is moving inevitably towards 'technocracy'. The argument is a good one, granted Dewey's philosophy, but is not pure factual description and scientific induction from it, as the author supposes. The irony of the situation is that Dewey in his political thinking is a good nineteenth-century liberal and far from drawing the conclusions that follow from his own philosophy.

If Dewey is the most characteristically American, the others of his generation are equally important.

Pierce, in spite of his obscurity and perversity, is the most original and stimulating thinker that America has produced. His work on logic and scientific method has scarcely been fully appreciated even in his own country. Now that idealism of the nineteenth-century type is unfashionable, Royce is apt to be dismissed as just one of those Hegelians, but he was a very individual one. What is more, that type of philosophy is far from being dead. Though there may be very little positive to be found in the philosophy of Santayana, yet his melancholy, detached, poetical survey of existence has provided some of the best criticism of modern errors and follies ever made, expressed in magnificent English. These are all men of the past generation, who attained maturity round about the turn of the century. In the present generation America has absorbed some half-dozen European philosophies, varying from Neo-Thomism to logical positivism. It is not very clear what the ferment of thought is now producing, especially at a time when books appear to have great difficulty in crossing the Atlantic; but there is very little doubt that it is productive.

It may be worth while to emphasize the fact, probably not fully realized by most, that there is now more philosophical activity and more work of high quality being published in the United States than in the whole of Europe. Whatever the causes, the centre of gravity of the philosophical world is no longer in Western Europe, where it has been for so many centuries. It may never return there again. This is an additional reason for welcoming Prof. Schneider's book.

A. D. RITCHIE

AN EARLY NINETEENTH CENTURY AMERICAN MEDICAL MAN

William Beaumont's Formative Years

Two Early Notebooks, 1811–1821. With Annotations and an Introductory Essay by Genevieve Miller. Pp. xv+88+21 plates. (New York: Henry Schuman, 1946.) 6 dollars.

OF all men who have made really important contributions to the science of physiology, William Beaumont was perhaps the only one who carried out the whole of his researches on a single patient. Born in 1785 in Lebanon, Connecticut, Beaumont eventually obtained a licence to practise medicine and enlisted as a surgeon in the U.S. Army. Ten years later—in 1822—while he was serving at Fort Mackinac between Lake Huron and Lake Michigan, an accident happened in the local store. A gun had been accidentally discharged, and a young French-Canadian had received terrible injuries from buckshot in his left side. This man, Alexis St. Martin, is surely the most famous of all patients. His recovery was slow and he was left with a gastric fistula. After ten months the authorities decided to wash their hands of him, and Beaumont took him under his own personal care. From time to time St. Martin escaped and led his own life, but he frequently returned. The relationship between doctor and patient was not broken until 1844. Beaumont saw soon after the development of the fistula the possibility of using St. Martin as a human laboratory. In 1833 he published at his own expense the work entitled "Experiments and Observations on the Gastric Juice and the Physiology of Digestion". It is one of the great classics of physiology.

Two notebooks of Beaumont have survived—both dating from the pre-St. Martin period, and both preserved in the Washington University School of Medicine. One book covers his medical notes and case histories; the other his jottings from books which he had read, notes on daily incidents in his life, and other items. Both notebooks have been quoted from previously, but they have now been reproduced *in extenso* in a single book, under the able editorship of Miss Genevieve Miller, of the Johns Hopkins Institute of the History of Medicine.

There is nothing of outstanding interest in the medical notebook, and the authors from which Beaumont makes notes were all widely read in his day. Names such as Haller, Sydenham, Huxham, van Swieten, Cullen and Brown (of the Brunonian System) are common. It is somewhat unusual in a notebook of this type to find six lines devoted to the sorrow with which the death of Miss Maria Allen was received by her sorrowing relatives. We may wonder whether Beaumont had himself been in some way particularly attached to the patient. In the campaign of 1812 against the British he gave a certain treatment for pleurisy and peripneumony, and he noted that he had had more than two hundred cases without a death. On the next page he compares his treatment, for another condition, with that of the surgeon of the 16th Regiment—to his own detriment. So we read of him performing four amputations and three trepannings after an engagement, and in his general notebook he describes the scene on April 27, 1813, after the attack on York Town, when he and his fellow surgeons cut and slashed for forty-eight hours, without food or sleep.

These notebooks foreshadow Beaumont's accurate observation and his enthusiasm for new scenes. The non-medical authors—Shakespeare, Robert Burns, Wolcott, Byron, and others—from whom he quotes are sound enough fare, but the quotations are scarcely the choice of a literary man. One judges that Beaumont was essentially the man of action.

Miss Miller is to be congratulated on the skill with which she has edited these notebooks, and the publisher on the production of a charming volume.

E. ASHWORTH UNDERWOOD

THE STORY OF PENICILLIN

Miracle Drug

The Inner History of Penicillin. By David Masters. Pp. 191+17 plates. (London: Eyre and Spottiswoode (Publishers), Ltd., 1946.) 10*s*. 6*d*. net.

IN order to write both an accurate and a vivid account of the development of penicillin, David Masters has interviewed many people who played leading and even subsidiary parts in this story. Of the leading characters, notably Fleming and Florey, we are given a short life-history and personal description. Other participants come into the narrative only to describe that stage in the research in which their contribution mattered most. Scraps of conversation at critical moments are presumably recollections by the speakers of what they are likely to have said, and the circumstances attending more important occasions include a mention that the decision by Florey and Chain to investigate the possibilities of penicillin was taken under a particular tree while walking through the University Parks at Oxford. Heatley's night vigil with the first experimentally treated mice, his subsequent encounter with

a Home Guard while cycling home, and the anxieties of his journey to the United States with Florey—anxiety for the safety of the cultures they took with them when temperatures on the southern flying-boat route were well above the optimum for *Penicillium notatum*—are episodes of the kind which enliven this narrative.

The specialized work of each investigator, chemist, bacteriologist, cytologist, and even X-ray crystallographer is put into terms more or less comprehensible by the average reader, as are the problems of large-scale manufacture. There is a great deal in this book about the production of penicillin, perhaps because the aim is to trace the story of its development, especially during the War, when production was the urgent need, both for the original laboratory and clinical trials, and later for the treatment of battle casualties. There is less about its clinical uses, although the chief of them are mentioned in one place or another. So thoroughly has the author culled his sources of information that even those who know a good deal about this subject are likely to find something new to them in what he has written. His story is a little over-dramatized—centrifuges spin "dizzily", diseases are "dread", and patients are "rescued from the grave"—but it is perhaps a little difficult to ration one's superlatives in writing of such an achievement.

Posterity will probably rank the discovery of penicillin as the greatest British contribution to medicine since Harvey, and the greatest of all time in view of the circumstances in which it was brought to fruition. Florey had no alternative to calling in the manufacturing resources of the United States if penicillin was to play its part in treating war casualties. The price we have paid is that the processes of its manufacture are now covered by a series of American patents. What might have happened if the work of the Oxford team had been undertaken ten years earlier? Apart from anything else, the recognition of penicillin as a chemotherapeutic agent in 1930 would probably have prevented the discovery of the sulphonamides, and so have rendered the world as a whole the poorer.

L. P. GARROD

A STUDY OF HUMAN ODDITIES

Some Human Oddities

Studies in the Queer, the Uncanny and the Fanatical. By E. J. Dingwall. Pp. 198+12 plates. (London: Home & Van Thal, Ltd., 1947.) 15*s*.

IN one sense this book might be considered as an entertaining series of erudite biographical trivia, but in his amusing and lightly written account of such figures as the levitating Saint Joseph of Copertino, D. D. Home, the sorcerer who was such a personage in Victorian social life, and Angel Anna, the priestess of an obscene occult sect, Dr. Dingwall has enshrined a scientific moral. This is, that before denying the existence of such phenomena as he describes, we should sift the evidence and use our reason rather than that prejudice, either of belief or disbelief, which is not confined to the laymen of science; and that—if we accept the evidence—instead of admitting that unaccountable things do happen and leaving it at that, we should use available scientific methods to understand them. For example, whether (if at all) the flights of Saint Joseph occurred through divine or diabolic agency, or whether through some unknown natural force, it seems probable that there were in his own person psychological and physiological concomitants amenable to modern methods of inquiry.

This is eminently reasonable, and in his use of evidence Dr. Dingwall has given a distinguished example of objectivity. His case studies, moreover, point out many lacunæ in our knowledge in the fields of medical, sociological, psychological and psychic research; but it is a pity that the subjects he has chosen have been so long dead that the application of scientific principles to their cases is no longer possible. Nevertheless, in the appendixes to each chapter, which are crammed with learning, offsetting the easy manner of the narrative, he has frequent recourse to the terminology of science, especially of modern psychopathology. This appears somewhat unsafe. In psychiatric diagnosis isolated symptoms can seldom be relied on, but must be related to the whole context of the individual's life, especially to the intimate circumstances of his infancy. We know, also, that in different cultural settings arise standardized modes of behaviour which in Great Britain we would stigmatize as psychotic or pre-psychotic, but which, in their own milieu, do not impair the ability of the persons concerned satisfactorily to manage their own lives. Therefore, to suggest the possibility of applying psychological techniques to the investigation of seventeenth- or even twentieth-century characters of whose formative early life we are almost totally ignorant, and whose social environment may have been very different from our own, seems misleading. It is true that Dr. Dingwall only suggests this possibility tentatively, but psychology, especially psychoanalysis, has suffered so much from the common distortions which have restored to it the function of wizardry as the modern solution to all mysteries and cure of all ills, that its limits must be widely recognized if its potentialities are to be realized. The same criticism might be levelled against hypotheses in terms of glandular abnormalities. We can know very little of the detailed clinical history of persons who lived before modern methods in medicine were evolved, and to attempt retrospectively to diagnose them is a facile abuse of the science employed.

What then is to be gained from studying these strange people from past centuries? The answer, perhaps, is that they provide some material for comparison with equivalent present-day happenings, occurring in a social framework of which we have direct knowledge, and which can be fully examined and tested. But to start with the unverifiable past, though in some ways stimulating and no doubt absorbing to the investigator, seems methodologically unfruitful.

It is to be regretted that Dr. Dingwall's penetrating mind and lively pen were not directed more towards some modern oddities. The transvestite, for example, is so relatively common a phenomenon, that research in any large city would have brought to light psychological and sociological facts far more revealing, if less entertaining, than those which he has presented. In addition, there are living to-day individuals widely credited with feats which might have made even Home feel jealous.

Nevertheless, Dr. Dingwall has given us a book full of strange and macabre facts of the type which, quite apart from their scientific significance, everyone finds fascinating; and for those who wish to make their own inquiries he has provided a very full bibliography and, above all, a scientific incentive.

WYE COLLEGE

FIVE-HUNDREDTH ANNIVERSARY

WYE COLLEGE was founded in 1447 by Cardinal Archbishop John Kempe, who was Archbishop of Canterbury and Lord Chancellor of England. He established his foundation in the township of his birth as a secular college of priests incorporating a grammar school. The foundation endured for one century only; but the educational tradition has persisted, finding its present embodiment in Wye College, now a school of agriculture and horticulture of the University of London.

The fifteenth-century quadrangle and its ancillary buildings survive in their main substance and retain many features of interest and charm. All are in use to-day; the original great hall, now the library, is particularly noteworthy. On the confiscation of the chantry endowments and lands in 1543, the King granted the estate to Sir Walter Bucler (secretary to Katherine Parr), but stipulated that there should be maintained "a master sufficiently erudite in grammar to teach boys and youths at Wye". Thus in part the wishes of the founder were respected. The provision was set aside by an owner in the seventeenth century, but was soon vindicated by Charles I and, apart from this one short break, teaching continued from the original foundation until the present day. The grammar school apparently never enjoyed any but local repute, though two of the grammar masters were figures of their time. The Rev. Johnson Towers, appointed in 1754, later became master of Tonbridge School, and the Rev. Philip Parsons, who followed Towers as grammar master, enjoyed some distinction as an antiquary in Kent. Rather strangely, a separate school occupied part of the buildings during 1713–1893. Established by Lady Joanna Thornhill for the children of the poor of Wye, this latter foundation survives to-day in new premises which form part of the State elementary school of the township.

In 1892 the County Councils of Kent and Surrey determined upon the establishment of an agricultural college. The governing body appointed as its first principal A. D. Hall (later Sir Daniel Hall), then a young university extension lecturer in the two counties. He had been a student of the natural sciences at Balliol College, Oxford, and in the rural atmosphere of the south-east soon came to realize what might be done by systematic, continuous and modern instruction in agriculture.

The Charity Commissioners presumably relinquished without regret the premises, expensive to preserve from decay, and scarcely suitable for elementary instruction. In 1894, Hall opened the College with a small group of seventeen students, and it was not long before new buildings were added to the College. Further substantial additions have been made from time to time in parallel with the growth of the College, and plans for further extensions are being developed to-day. At first the College had no farm of its own, but the governing body soon realized the importance of a farm both for purposes of demonstration and for investigations. A farm contiguous with the College was taken, and land gradually added to, until to-day the College is farming more than 600 acres which includes hop gardens, orchards, and market gardens, as well as a mixed farm typical of east Kent conditions. The College estate forms the laboratory of agricultural and horticultural teaching, but it has been managed so that sight has never been lost of the importance of inculcating and demonstrating good sound commercial practice. The financial success with which the farming enterprises have been conducted has done much to establish the good name of the College among the local agricultural community.

In the last fifty years a number of men of distinction have been associated with Wye. Among these the first principal is pre-eminent. He left Wye in 1902 to become director of Rothamsted Experimental Station. Among his colleagues at Wye may be mentioned F. V. Theobald, the well-known entomologist; John Percival, who later became professor of agricultural botany at Reading; and Sir John Russell, who collaborated with Hall in so much of the latter's earlier work at Wye and who later followed him as director of Rothamsted. Among the small band of early students at the College was C. S. Orwin, the first treasurer of the College Union Society. He was a member of the College teaching staff for three years, and later became the first and distinguished director of the Agricultural Economics Research Institute of the University of Oxford. Dr. C. D. Darlington, the present director of the John Innes Horticultural Institution, is another distinguished student of the College who himself follows in Hall's footsteps in his present appointment. But probably the best witnesses to the work of Wye College are the large number of successful practical men—farmers, growers and agricultural administrators—to be found all over the south-east of England and, indeed, in most parts of Britain, as well as scattered throughout the Empire and beyond.

From its early days the College has been the centre of numerous agricultural investigations, largely suggested by local agricultural practice and need. The hop plant, so typical of the country in which Wye stands, has always occupied an important place in the activities of the College. Hall himself became interested in the plant, and it was early in the century that E. S. Salmon was appointed as mycologist to the College. It was through the work that he did in connexion with the control of downy mildew that he has become primarily interested in hop problems, and his long and distinguished career has gained for himself and for the College an international reputation. In east Kent, fruit occupies a singularly important place in the rural economy, and it is only natural that the study of pomology should have developed early at Wye College. It is sometimes forgotten that East Malling Research Station, which now occupies an important position in the scientific world, was founded in 1912 as the Wye College experimental fruit station, since the land at East Malling was considered to be more suitable for experimental work than that available in the immediate environment of the College. After about five years its direct connexion with its parent body was severed, and it started on an independent and successful life.

It was soon after the end of the First World War that the specialist agricultural advisory services were established, and it was natural that Wye, which had already had a distinguished career as the local agricultural centre, should have become the advisory centre for the south-east of Great Britain. For twenty-five years the College was responsible for conducting agricultural advisory and research work in the locality. This type of work which Wye College had been so instrumental in developing has now been taken over by the newly established National Agri-

cultural Advisory Service, but the connexion between the Service and the College is preserved in that the new centre is being built on College property and will remain in the closest association with its parent body.

Between the two World Wars, student numbers at Wye varied between 160 and 180, and indeed in one year passed 200. At the beginning of the recent War it was impossible to continue teaching at the College. Some of the students completed their courses at the University of Reading, others left to join the Services, and the building was occupied by the Army. As soon as it became possible to foresee the re-opening of the College, the governing body entered into discussions with the Ministry of Agriculture and with the governing body of Swanley Horticultural College for Women, which had put forward the suggestion of amalgamating with the South-Eastern Agricultural College at Wye. The two institutions had been in many respects complementary and had been associated in some aspects of their work. Swanley College, founded in 1888, had already won for itself a position of outstanding importance in the horticultural world, particularly under the able leadership of Dr. Kate Barratt, who was principal of the College from 1922 to its final closure in 1945. Swanley College, although originally opened for men, became a women's college soon after its foundation. During the War it was severely damaged by enemy action, and staff and students were driven from home, but continuous teaching was maintained, albeit on a somewhat reduced scale and under very great difficulties. It seemed a perfectly logical step that the two Colleges should amalgamate, and the amalgamation was, in fact, accomplished in 1946, and Wye College opened for the teaching of both men and women students in agriculture and horticulture, with Mr. Dunstan Skilbeck as its principal.

This grafting operation produced fruitful results. At present there are 140 students, and only the problem of building new accommodation hinders its early expansion to 200 or more. The link with the University of London, of which the College is part, is becoming increasingly strong, and the academic status of the College has recently been advanced by the institution of chairs of agriculture and horticulture, to which the University of London has appointed respectively Mr. M. McG. Cooper and Dr. H. W. Miles.

At the present time, undergraduate teaching is restricted to the B.Sc. degree courses of the University of London in agriculture and horticulture; but, in spite of the sound introduction to the basic sciences which is given in the present curricula, sight is not lost of the more practical aspects of the two studies. There is perhaps a danger at times that in studying the applied sciences and crafts there is a tendency for the work to become too academic; but Wye College, lying amid its green fields and pleasant gardens, is scarcely likely to neglect what is, after all, the fundamental objective of the study of agriculture and horticulture. The present syllabus is now under review and will almost certainly be extensively revised once the University of London has determined its policy with regard to matriculation and intermediate examinations.

Built upon the sound and distinguished traditions of its predecessors, Wye College has a very large part to play in the future development of agriculture and horticulture, not only in Great Britain but also throughout the British Empire. An important function of the College will be to train those who will become competent in the management of land and leaders of the joint industries of agriculture and horticulture. It will also concentrate upon the training of agricultural administrators for service both at home and overseas. Its work, however, will not stop with such training. The great developments which have occurred in agriculture and horticulture during the past two decades or so demonstrate the need of an increasing number of well-trained post-graduate workers, and it is hoped to build up at Wye a strong post-graduate school for the further training of those who have already received their initial training in the discipline of one of the basic sciences.

Medieval institutions have survived for the most part only by adaptation to the changing needs of society. It is not pretended that members of Wye College to-day are the full inheritors of Kempe's endowment; but they continue a line of scholarship which extends from his foundations. They preserve in the buildings which he erected some measure of his intentions, in the fulfilment of developments which he could not himself have envisaged.

REACTION BETWEEN CATALASE AND HYDROGEN PEROXIDE

By Dr. P. GEORGE

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WHEN catalase is added to hydrogen peroxide, there is an initial rapid evolution of oxygen which lasts for about two minutes, depending on the peroxide concentration. After this, oxygen is given off at a steady rate which slowly decreases in the course of an hour. This decrease in the rate is undoubtedly due to enzyme destruction, and several kinetic equations have been developed to account for it[1]. The rapid evolution and the steady rate, however, are inherent features of the peroxide decomposition.

The kinetics of the reaction with erythrocyte catalase in phosphate buffer *p*H 5·85 were determined using Barcroft manometers and also a modified 'boat technique' with a pressure gauge for measuring rapid rates. Fig. 1*A* shows how the total oxygen is evolved in an initial rapid reaction completed in about two minutes and a steady reaction which occurs simultaneously. The correction for the blank reaction was found to be negligible. In the initial reaction the rate of oxygen evolution was found to decrease exponentially with time. This exponential decrease was more rapid the higher the peroxide concentration, according to the following expression for the first-order constant k_1 (sec.$^{-1}$), which was independent of the catalase concentration:

$$k_1 = \frac{aP}{b + P} + cP,$$

where P is the peroxide concentration in moles per litre, and a, b and c are constants having the values 0·072 litre sec.$^{-1}$ mole^{-1}, 0·15 mole litre^{-1} and 0·0185 litre sec.$^{-1}$ mole^{-1} at 0° C. respectively.

The total amount of oxygen evolved in the initial reaction (ΔO_2 in Fig. 1*A*) was found to be many times greater than the amount of catalase present, that is, between 5·8 × 10^5 and 4·0 × 10^6 moles oxygen per mole catalase, depending on the peroxide

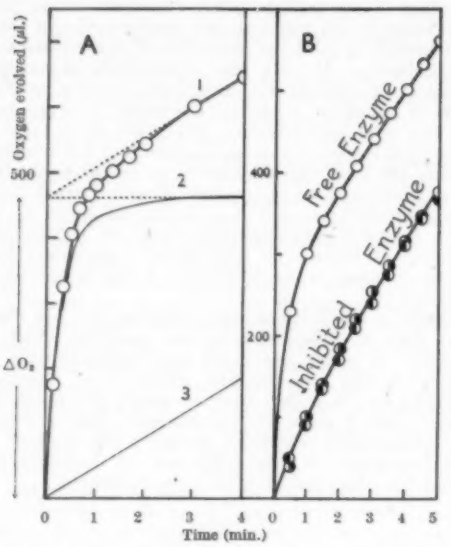

Fig. 1

A: Oxygen evolution from 0·5 *M* hydrogen peroxide in phosphate buffer *p*H 5·85, with erythrocyte catalase at 0° C. The observed Curve 1 is shown as the total oxygen evolved in an initial reaction 2 and in a steady reaction 3. The initial reaction is finished in about two minutes after an evolution of oxygen given by ΔO_2. *B*: Oxygen evolution from 0·5 *M* hydrogen peroxide in phosphate buffer *p*H 7·3, at 20° C. with the free enzyme (open circles) and the enzyme inhibited by $1·3 \times 10^{-4}$ *M* potassium cyanide (right-hand shaded circles) and by $2·0 \times 10^{-7}$ *M* sodium azide (left-hand shaded circles)

concentration. From the values of ΔO_2 and k_1, the true rate of oxygen evolution R_r at the beginning of the initial rapid reaction can be calculated. R_r was found to be directly proportional to the catalase concentration and to show the complex variation with peroxide concentration illustrated in Fig. 2, with a marked maximum rate at about 0·4 *M* hydrogen peroxide. The steady rate R_s showed similar behaviour (Fig. 2), only in this case the maximum rate occurs at about 0·07 *M* hydrogen peroxide. These results show a strong inhibition of the peroxide decomposition at high peroxide concentrations. Similar results were obtained with specimens of liver catalase and lysed red blood cells, and further experiments showed they could not be attributed to the presence of inhibitors in the peroxide or the nature and concentration of the buffer solution used. The inhibition at high peroxide concentrations was shown to be quantitatively reversible by experiments in which dilute buffer solution or small amounts of 100 vol. hydrogen peroxide were added during the course of the reaction. Enzyme destruction therefore plays no part in determining these kinetic relationships.

Experiments carried out using sodium azide and potassium cyanide to inhibit the catalase showed two striking features. First, low azide concentrations (about 2×10^{-7} *M*) and low cyanide concentrations ($1·3 \times 10^{-4}$ *M*), which do not affect the steady rate of oxygen evolution, almost eliminate the initial rapid reaction (Fig. 1*B*). Higher inhibitor concentrations were found to eliminate it completely and also decrease the steady rate. Secondly, at high azide concentrations (0·6 *M*) the enzyme is still active, but the kinetics of the peroxide decomposition differ from those of the uninhibited reaction. The variation of the inhibited rate *R'*, with peroxide concentration no longer shows a maximum but increases with increasing peroxide concentration (Fig. 2).

While this kinetic investigation gives no direct evidence for the mechanism of the oxygen evolution, the following conclusions can be drawn concerning the part that catalase plays in the reaction. First, in the presence of hydrogen peroxide, catalase can exist in two forms, a labile and more active form present during the initial rapid evolution of oxygen, which changes in about two minutes to a stable and less active form responsible for the slower steady oxygen evolution. The change is reversible, and so it cannot be caused by partial enzyme destruction. Secondly, cyanide and azide react with the more active form and completely eliminate the initial rapid reaction at concentrations too low to affect the steady rate. Thirdly, the peroxide decomposition by strong azide catalase shows no inhibition by peroxide itself, which suggests that the inhibition of the free enzyme by peroxide is due to the formation of a peroxide complex having a lower catalytic activity. In azide-catalase an azide complex is already formed and so no inhibition by peroxide can be observed.

With the present kinetic data it is only possible to discuss the action of the enzyme in general terms. To explain the ready combination of azide and cyanide with the more active form and the inhibition of the free enzyme by peroxide itself, it is necessary to assume a twofold interaction between the enzyme and either peroxide or inhibitor, such that when one peroxide or inhibitor molecule has combined, the enzyme is still catalytically active. This can happen in two ways. On one hand, the iron in the hæmin group may not be directly attached to the protein in all phases of the reaction, and so be capable of combination with two substrate molecules as it is in free hæmin or hæm. In this mechanism each of the four hæmin groups in the erythrocyte catalase acts independently. On the other hand, if the iron in the hæmin group is directly joined to the protein and can

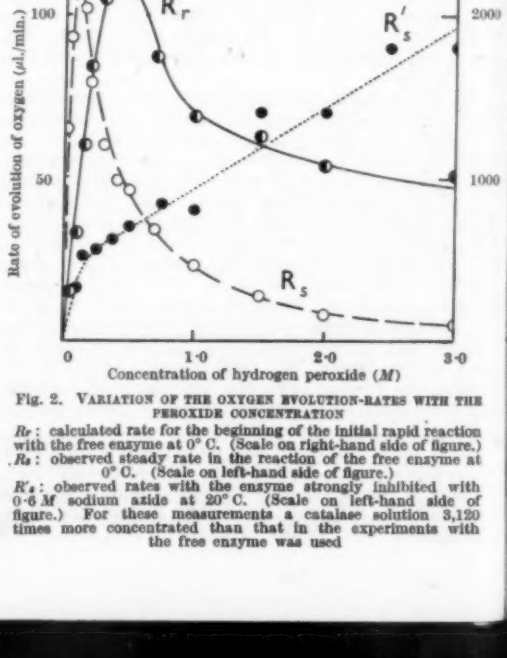

Fig. 2. VARIATION OF THE OXYGEN EVOLUTION-RATES WITH THE PEROXIDE CONCENTRATION

R_r: calculated rate for the beginning of the initial rapid reaction with the free enzyme at 0° C. (Scale on right-hand side of figure.) R_s: observed steady rate in the reaction of the free enzyme at 0° C. (Scale on left-hand side of figure.)

R'_s: observed rates with the enzyme strongly inhibited with 0·6 *M* sodium azide at 20° C. (Scale on left-hand side of figure.) For these measurements a catalase solution 3,120 times more concentrated than that in the experiments with the free enzyme was used

only combine with one substrate molecule, the results can be explained by assuming a powerful hæmin-hæmin interaction which causes the affinity and catalytic reactivity of the remaining free hæmin groups to decrease when one group is held in combination.

The formation of a hæmin-peroxide complex is implicit in both mechanisms, and a possible explanation for the transition from the initial rapid rate to the steady rate lies in the setting up of an equilibrium between the hæmin peroxide complex and its decomposition product. The equilibrium in both cases is one between opposing first-order reactions with respect to the hæmin group. The amount of oxygen evolved while such an equilibrium is being reached should decrease exponentially, which is in agreement with experiment; and furthermore, it can be shown that the first-order constant k_1 should be made up of the constants for the forward and back reactions. The forward reaction can be identified with the term $aP/(b + P)$, and the back reaction with cP. The forward reaction thus corresponds to the decomposition of the hæmin-peroxide complex, and the back reaction to a regeneration of the hæmin group by reaction with another peroxide molecule.

Forward reaction: $E + P \rightleftharpoons EP$ (rapid equilibrium)
$EP \rightarrow E' +$ products (rate-determining step).
Back reaction: $E' + P \rightarrow E +$ products (rate-determining step).

The familiar valency change of a ferric iron atom provides the simplest chemical picture for these general reactions. The labile more active form of the catalase may thus be identified with an equilibrium mixture of the ferric enzyme and its peroxide complex, and the less active form of the catalase with an equilibrium mixture of ferric enzyme, peroxide complex and ferrous enzyme.

If the total amount of oxygen evolved while the equilibrium is being set up (ΔO_2 above) comes entirely from the forward and back reactions, then the ratio $\Delta O_2/E$, where E is the enzyme concentration, should be less than one. The experimental values for this ratio lie between $5{\cdot}8 \times 10^5$ and $4{\cdot}0 \times 10^6$. These high values could arise from a chain decomposition of the peroxide: however, it has as yet been impossible to set up any chain mechanism which would account for the observed kinetics, and an explanation in terms of the alternative mechanisms proposed above may be considered. First, if each hæmin group can combine with two peroxide molecules, then the high values of $\Delta O_2/E$ can be explained by the rapid reaction of one combined peroxide molecule while equilibrium conditions are being reached in the reactions of the other. Secondly, if each hæmin group can react only with one peroxide molecule, the high values of $\Delta O_2/E$ can be explained by the rapid reaction of the three remaining hæmin groups with peroxide while equilibrium conditions are reached in the reactions of the first hæmin group. This second explanation seems more likely, because it is easier to understand the great catalytic power of catalase if its hæmin iron atoms are directly joined to the protein during all phases of the reaction. The assumption of differing reactivities of the four hæmin groups of catalase would bring the enzyme into line with hæmoglobin, where it is necessary to assume that the four hæm groups have differing affinities for oxygen to explain the sigmoid shape of the dissociation curve[2].

A full account of the kinetics of the uninhibited reaction is in the process of publication, and further experiments are being carried out on the reaction inhibited by cyanide and azide to determine whether any differences exist in their kinetic effects. The resemblance between the action of the two inhibitors reported above is very remarkable in view of the contrasting spectroscopic and chemical properties of azide-catalase and cyan-catalase shown in the experiments of Keilin and Hartree[3].

[1] Yamasaki, E., *Tôhoku Imperial Univ., Sci. Rep.*, **8**, No. 13 (1920). Morgulis, S., *J. Biol. Chem.*, **47**, 341 (1921). Northrop, J. H., *J. Gen. Physiol.*, **7**, 373 (1924–25). Williams, J., *J. Gen. Physiol.*, **11**, 309 (1927–28).

[2] Adair, G., *Proc. Roy. Soc.*, A, **103**, 627 (1925). Adair, G., *Proc. Roy. Soc.*, A, **109**, 292 (1925). Perry, R. M., and Green, A. A., *J. Biol. Chem.*, **81**, 175 (1929).

[3] Keilin, D., and Hartree, E. F., *Proc. Roy. Soc.*, B, **121**, 173 (1936).

VLADIMIR N. IPATIEFF

THE memoirs of Prof. Vladimir Ipatieff are written in the grand manner*. They cover a period of sixty years, during which the author not only achieved distinction in the field of chemical research but also, at the same time, played an important part in the great revolution and renaissance of his country. On all the stirring events in which he was a prominent actor, he throws an illuminating and revealing light.

Born in 1867, Ipatieff had grown to manhood and had acquired a European reputation at the time the Tsar signed the famous Manifesto of October 17, 1905, and when the first Duma met in the spring of the following year. For a short space, there seemed a fair prospect of Russia becoming a constitutional monarchy. "My eyes filled with tears," says Ipatieff, "when I read the Manifesto. I could hardly believe that I was witnessing my country's entrance into the path of political development long since entered by other Western Countries." But the dawn of this hopeful era was soon overcast. A powerful aristocracy and a corrupt court were not prepared to lose their inherited privileges without a struggle. Political, religious and domestic pressure was brought to bear upon the Emperor, and he failed to withstand the combination. An internecine struggle between the old order and the growing revolutionary movement followed. A Soviet of Workers' Deputies was organised by Trotsky and Khrustalev; open revolt occurred in many districts, and massacres and deportations followed. A semblance of order was restored, and it took another decade of misrule and the impact of a world war to precipitate that final explosion of popular resentment, which has since had such world-wide consequences.

During that uneasy interval which preceded the First World War, Ipatieff pursued his scientific research with great concentration and with outstanding success. His investigations of catalytic reactions and his discovery of the precipitation of metals from their salt solutions by the action of hydrogen at high pressure date from this period. But as the great crisis of his country approached, he became increasingly involved in its industrial affairs. His administrative and technical abilities were soon recognized and, by 1914, we find him, as a prominent member of the Artillery Committee of the Chief Artillery Administration, largely responsible for the planning of industry throughout the Russian Empire.

* The Life of a Chemist: Memoirs of Vladimir N. Ipatieff. Edited by Xenia Joukoff Eudin, Helen Dwight Fisher and Harold H. Fisher. Translated by Vladimir Haensel and Mrs. Ralph H. Lusher. (Hoover Library on War, Revolution and Peace, Publication No. 21.) Pp. xv+658+8 plates. (Stanford University, Calif.: Stanford University Press; London: Oxford University Press, 1946.) 33*s.* 6*d.* net.

The energy, enterprise and judgment he displayed during the difficult war years would be considered exceptional, even in one trained to important administrative tasks. That they should be found in a man of science brought up in academic seclusion and long confined to the narrow paths of fundamental scientific research may be thought a portent.

On this subject, the memoirs are singularly revealing and present an interesting psychological study. Perhaps the main characteristics of the author may be summarized as an abiding enthusiasm for scientific studies, a deep sincerity of purpose and abounding self-confidence. From that day in early youth when, with some trepidation, he waited upon the great chemist Mendeléeff and received from the lips of the sage an opinion that his knowledge was too meagre for experimental work, until the occasion some thirty-five years later when he celebrated his scientific jubilee amid congratulations from the whole scientific world, no misgivings ever entered his mind as to his high destiny. Indeed we may attribute to this trait an impatience with mediocrity and a highly critical attitude towards his colleagues and associates, which form one of the less pleasing aspects of his character.

The Revolution of 1917 found Ipatieff a lieutenant-general in the Imperial Russian Army, chairman of the important Chemical Committee and one of the key men responsible for the organisation and conduct of the industrial war effort. From the first, he refused to interest himself in political affairs, but was prepared to work loyally with any party in power. There were moments in those turbulent days which ushered in the spring of 1917 when it seemed probable that he would share the fate of his distinguished predecessor, Lavoisier. The revolutionaries of the Kremlin had no greater respect for savants than had those of the Luxembourg; many of his colleagues perished in the first explosion of popular wrath. But Ipatieff had powerful friends and loyal subordinates. "During the first days of the Revolution," he says, "the soldiers of the Chemical Battalion were worried about me and repeatedly offered their protection in case of danger." He continued to be employed by the Provisional Government, and later by the Bolsheviks, under Lenin. Although an uncompromising individualist, he contrived to work with the People's Commissars and with the Party representatives on his various committees. But his opinion of his colleagues is outspoken and critical. Of Kuibyshev, chairman of the Supreme Council of National Economy, he says: "I knew no more narrow-minded, stupid man than he. His knowledge of industry was nil, and, since he had no opinions of his own, his superiors could easily persuade him to accept theirs. I did not like him, nor he me." Of another eminent colleague, Lobov, he states: "His stupid, unattractive face classified him at once as one fitted for only the most menial work".

Holding these views, which he was not always successful in concealing, it is not surprising that he encountered increasing political obstruction in his efforts to organise and develop the Russian chemical industry in the post-war years. While Lenin and Trotsky were in power his position was assured; but Lenin was a sick man, and after his death Trotsky's influence declined, and he was finally expelled from the Party and exiled in 1927. Of all the revolutionary leaders with whom Ipatieff came in contact, Lenin impressed him as being the only one with the high ideals and vision necessary to build up the new Russia on sound and progressive lines.

Stalin succeeded Lenin and, under his leadership, the Soviet Government gradually assumed its present form. The State Political Administration, afterwards the G.P.U., was created in 1922, and rapidly grew to be a powerful instrument of Government policy. Ipatieff's position became increasingly dangerous. His refusal to join the Party, his outspoken criticism of his political colleagues and his frequent visits abroad served to arouse the suspicion of the G.P.U. Many of his contemporaries were arrested and imprisoned or executed. "I reckoned," he says, "that up to 1930, of all the military engineer-technologists who had completed their training at the Artillery Academy, only two or three were left in Soviet territory. The remainder had been arrested and their fate was unknown. Day by day, these facts confirmed my suspicions that I could not long escape the fate of most of my dear students and comrades of the Artillery Academy."

He resolved to quit Russia for ever. Fortunately, he had duties which necessitated frequent visits to Germany; and, in June 1930, he was able to obtain permission again to proceed there on Government business. It was with a feeling of relief and gratitude that, in company with his wife, he passed the frontier for the last time; and on this happy note the memoirs end. It is gratifying to know, however, that after so many years of trouble and danger, Ipatieff spent his declining years a distinguished and honoured guest of the United States. D. M. Newitt

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OBITUARIES

Sir F. Gowland Hopkins, O.M., F.R.S.

Frederick Gowland Hopkins, the father of British biochemistry, and perhaps the last of our great pioneers of science, died on May 16, at the age of eighty-five. His death will be felt with a keen sense of loss by all those who have come under his inspiring influence.

Hopkins was born at Eastbourne on June 20, 1861, in a house now destroyed by enemy action. While still an infant he lost his father, who had been an enthusiastic amateur in science. This loss greatly affected his subsequent career. He was educated at private schools. He published his first scientific contribution—a brief note—at the age of seventeen. Shortly afterwards he was articled to a public analyst, from whom he received his first technical training, and in 1883 he was appointed assistant to Sir Thomas Stevenson, the eminent Home Office analyst, whose evidence played an important part in many sensational trials. His real scientific education, however, began five years later, when at the late age of twenty-seven he became a medical student at Guy's Hospital. The ordinary medical curriculum constituted his only academic training. During his medical course he did important research and was the first holder of the Gull Research Studentship. He graduated in science and medicine at the University of London in 1894, and was a member of the staff of Guy's Hospital Medical School.

In 1898 Hopkins married Jessie Stevens, daughter of Edward Stevens, of St. Lawrence, Kent, and was expecting to follow a clinical career. In the same year, however, Sir Michael Foster invited him to join the staff of the physiological department at Cam-

bridge, with the task of developing and extending the teaching of the chemical side of physiology in the University. Here he held a University lectureship in physiology for some years. He was elected a fellow of the Royal Society in 1905. During 1905–10 he was tutor of Emmanuel College. In 1910 Trinity College offered him a fellowship and appointed him prælector in physiological chemistry, and in the following year he was made University reader in chemical physiology.

Up to this time the physiological chemistry department at Cambridge had formed a section of the physiology department; but in 1914 a special chair of biochemistry was created for Gowland Hopkins and a separate biochemical department was formed. In 1921 a large bequest from the trustees of Sir William Dunn made it possible to provide a separate building and staff for the new department. The building, accommodating about forty research workers, was completed in 1924, and under Hopkins' leadership a large and active school of biochemistry rapidly grew up and has played an important part in the development of the subject. He was knighted in 1925, and shared the Nobel Prize for Physiology and Medicine in 1929 "for his discovery of growth-promoting vitamins". During 1930–35 he was president of the Royal Society, and in 1935 he received the Order of Merit. He received many other honours, including doctorates from more than twenty universities. He retired in 1943, having held the professorship of biochemistry at Cambridge for thirty years. Such, in bare outline, was his career.

Hopkins made many fundamental contributions to biochemistry. Throughout his life and amid all his duties, he always managed to find time to keep his research going, though sometimes only with difficulty. He never wrote a book, but his scientific papers form a series extending over seventy years, from his first, published in 1878, to his last, sent in only a month before his death, and now in the press. He had considerable literary gifts, and many of these papers make delightful reading; it is fascinating to read them in chronological order and to follow the gradual development of his work and thought.

As a young man Hopkins was an enthusiastic collector of butterflies, moths and beetles. In 1878 there appeared large numbers of the little bombardier beetle, which ejects a cloud of violet vapour into the air when attacked. Hopkins was curious to know what this stuff could be; he showed that the vapour could be condensed in a test-tube, but at that time lacked the chemical knowledge to determine its nature. Fifty-seven years later, commenting on this, he said, "I think, however, that from that time my fate was sealed. Though the designation was not yet invented, I became there and then a biochemist at heart."

His first real chemical research, carried out between 1881 and 1895, was on the pigments of the wings of butterflies, and resulted in the discovery of the class of compounds now known as pterins, which recent work suggests may have important functions in the animal body also. Hopkins showed that they are closely related in chemical structure to uric acid, though their exact constitution remained undetermined for fifty years more. He returned to this subject near the end of his life, making further interesting observations.

This early work interested him in uric acid, to which much importance was then attached in medical circles, and he introduced in 1893 a method for its estimation in urine, which remained the standard method for many years. He studied its excretion in various diseases, and published papers on the effect of various diets on its metabolic production. This was before the stages of nucleic acid breakdown had been made clear. Much later, in 1922, he made a further contribution to this topic by his discovery that milk contained large amounts of the enzyme which forms uric acid, namely, xanthine oxidase, upon which much work was later done in his laboratory.

In 1896 Hopkins became interested in proteins, apparently as a result of a chance observation that bromine quantitatively precipitated albumin from pathological urine. He prepared a number of halogenated proteins and gave reasons for believing that the halogen atoms were in the tyrosine rings. During this work he made a fundamental advance by devising a procedure for the easy and rapid preparation of crystalline proteins in reasonable amounts. Hofmeister's earlier method (by evaporating alkaline solutions containing ammonium sulphate) only yielded crystals with difficulty, and these were mixed with much amorphous protein. By adjusting the *p*H without evaporation, Hopkins obtained at once wholly crystalline material and showed that the product after recrystallization had the constant optical and other properties characteristic of a pure substance. This began a new era in protein investigation, and the method is now extensively used for the preparation of pure enzymes and other proteins.

Continuing his work on proteins in three classical papers with his pupil, S. W. Cole, Hopkins next investigated the Adamkiewicz protein colour-reaction (a purple colour on addition of acetic acid and sulphuric acid), which was believed to be a furfural reaction due to a carbohydrate group. They first showed that the test was due to glyoxylic acid present in the acetic acid and not to the acetic acid itself. Following up the substance responsible for the test, they succeeded in 1903 in isolating it by an elegant method from tryptic digests of protein as a beautifully crystalline product, which proved to be a new amino-acid and to be identical with "the much-sought tryptophane". 'Tryptophane' had been the name given to the hypothetical substance in protein hydrolysates which gave the red colour on addition of bromine-water, but previously it had been nothing more than a name.

The year 1905 and those immediately following were especially fruitful. The occurrence of the indole ring in tryptophane had raised the question in his mind whether the animal body could synthesize the amounts it required or whether the ring must be supplied preformed in the diet. To decide this he made use of zein, a protein which does not contain tryptophane, and in a celebrated pioneer paper in 1906 reported that a diet containing zein as the only protein was unable to maintain growth in young mice, but that the addition of tryptophane greatly prolonged their survival period. Addition of tyrosine (already present in zein) had no such effect. It was suggested that the tryptophane was utilized as the normal precursor of some specific 'hormone' or other substance essential to the processes of the body. From this arose the subject of 'essential amino-acids', which is so important to-day.

It was but a step from this to his work on vitamins, for which Hopkins became most widely known, though it was only a fraction of his whole research output. In 1905, in order to see whether there were other

previously unrecognized essential dietary factors, he fed synthetic diets, containing all the known essential foodstuffs, but carefully purified. To them he added small quantities of meat extracts or extracts from yeast to give flavour to the tasteless food. He was thinking then of the animal's 'appetite'. He quickly found, however, that rats ate synthetic diets very well without such additions. But the extracts powerfully affected nutrition: on the flavoured purified diet the animals grew well; without the flavouring there was continuous loss of weight, although they ate the same amount of food. He reported some of these epoch-making results in an address to the Society of Public Analysts in 1906, beginning modestly with the words:

"Seldom, I imagine, has this learned society welcomed a visitor less obviously entitled to occupy its time." But already at this early date the essential conception of vitamins was clear in his mind. "No animal can live upon a mixture of pure protein, fat and carbohydrate, and even when the necessary inorganic material is carefully supplied the animal still cannot flourish. The animal body is adjusted to live either upon plant tissues or the tissues of other animals, and these contain countless substances other than the proteins, carbohydrates and fats. Physiological evolution, I believe, has made some of these well-nigh as essential as are the basal constituents of diet. . . . The field is almost unexplored; only is it certain that there are many minor factors in all diets of which the body takes account. In diseases such as rickets, and particularly in scurvy, we have had for long years knowledge of a dietetic factor; but though we know how to benefit these conditions empirically, the real errors in the diet are to this day quite obscure. They are, however, certainly of the kind which comprises these minimal qualitative factors that I am considering."

Publication of the results in full was, however, delayed until 1912 by prolonged but unsuccessful efforts to isolate the active substances. Hopkins never claimed to be the 'discoverer' of vitamins, though he might have done so with good reason; but it was certainly the 1912 paper which first awakened a general belief in the physiological significance of these substances. The battle was not won without a fight, and even so late as 1920 there was considerable opposition and scepticism towards the 'vitamin theory', especially on the part of a section of the medical profession. During the First World War, however, Hopkins had a great influence for good as chairman of official committees on wartime nutrition and famine relief, which did much important work. He frequently emphasized the inadequacy of a mere calorie figure as an index of nutritional standard—a lesson which seems in danger of being forgotten in some quarters at the present time.

In 1907 Hopkins also made, in collaboration with Fletcher, a most fundamental contribution to muscle biochemistry by showing that the production of lactic acid was intimately connected with the contraction of the muscle, and that it was removed once more by oxidation in presence of oxygen. This opened up a very large and fruitful field of work on tissue metabolism, on the glycolytic and oxidizing enzyme systems, and on the contraction process itself.

His next outstanding achievement was the discovery in 1921 of glutathione, the sulphur-containing peptide which is responsible for the nitroprusside reaction given by animal tissues. The isolation was long and difficult and the product non-crystalline, but Hopkins was able to show that it functioned as a catalyst in biological oxidation processes, becoming alternately oxidized and reduced and so acting as an intermediate 'hydrogen carrier'. This first directed attention to the importance of such carriers, which occupy a prominent place in tissue respiration systems to-day, and stimulated much research which made Cambridge thereafter one of the main centres of the study of biological oxidations.

At that time Hopkins believed glutathione to be a dipeptide of cysteine and glutamic acid, but in 1927 two American workers suggested the presence of a third component, possibly serine, though not in the form of a tripeptide. Hopkins immediately re-investigated the matter, and in a very short time had devised an unusual but wonderfully elegant method by which in a single step glutathione was precipitated from crude extracts as a pure salt, which immediately yielded the beautifully crystalline peptide. This at once made it readily accessible for research, and Hopkins showed conclusively that it was a tripeptide of cysteine, glutamic acid and glycine. Later, he published two papers on the part played by ascorbic acid in catalysing the oxidation of glutathione.

In 1930 he studied the production of thiol groups during the denaturation of proteins by strong solutions of urea. In 1938 he discovered that the enzyme which oxidizes succinate depends for its activity upon thiol groups within its molecule; this stimulated much further work, and many '—SH enzymes' have now been found.

Meanwhile, Lohmann had shown that glutathione is the specific coenzyme of the enzyme glyoxalase, and Hopkins later took up the study of this enzyme. His last paper, now in the press, reports the discovery that the glyoxalase system contains a hitherto unsuspected protein activator, apparently of a new type.

Throughout his life Hopkins retained a remarkably sure instinct for selecting problems which would yield important results. All his papers, from first to last, contain results of much interest, and many opened up new fields of research.

Hopkins' influence on the growth of biochemistry, however, was by no means confined to the results of his own personal research, important though they were. He had a great gift of inspiring others to do fruitful work, and from the Cambridge school which he created has come a great body of research which has played a fundamental part in the development of modern biochemistry. From it, too, has come a steady stream of research workers who have played a considerable part in the development of biochemistry in other centres in many parts of the world. It is interesting to look through a list of those whose names are well known in the biochemical world to-day, and to note how many have worked in Hopkins' laboratory at one time or another.

He also exerted a considerable influence through many important presidential and other addresses, which he delivered from time to time, on the nature and potentialities of biochemistry in its various aspects. Some thirty of these were published in various journals; they are all interesting and many are accepted as classics. In several he laid great stress on the importance of the dynamic side of biochemistry —the study of processes and reactions in living matter, and not merely of chemical structure. He was never

satisfied with knowing what a substance *was*, but always wanted to know what it *did*. It was natural, therefore, that he attached great importance to the specific enzyme catalysts within the living cell which bring these reactions about, and encouraged research on them in his department.

"I will ask you to consider," he said in 1931, "whether catalysis on highly specific lines is not among the most fundamental and significant phenomena in Nature"; and later, "I myself would like to claim that the control of events by intracellular enzymes, exerted in the specialized colloidal apparatus of the cell, by itself secures the status of the cell as a system which can maintain itself in dynamic equilibrium with its environment. I am not denying for a moment that the cell has esoteric qualities which may call for organising influence of a greatly different kind, exerted maybe at some higher level. It is at any rate sure that the inter-related activity of highly specific catalysts represents a notable device of Nature which has supported during the course of evolution those dynamic manifestations which characterize living things."

Hopkins was the kindest and most lovable of men. I still have a vivid recollection, after twenty-seven years, of the kindness of his first welcome to me when I joined his Department, and it was the same with all his pupils and colleagues, by all of whom he was greatly beloved. He never made an unkind or irritable remark; though he could be critical on occasion, it was always with a courtesy that left no sting. He had great charm of manner and was invariably courteous, even to the least important of us. He was always ready to talk over our work and ideas, and somehow contrived to make us feel by the way he listened to us that our ideas were extremely interesting and our results important. A great many of the papers published from his Department carry a note bearing witness to his "inspiration and encouragement". It has been said by critics that he suffered fools gladly and all his geese were swans; but the fact is that many of them did actually turn out to be swans, and it was impossible to remain a fool for long in his company.

Under Hopkins' leadership an unprecedentedly wide range of topics was covered, both in research and teaching, and a one-year whole-time course of instruction in advanced biochemistry was developed in Cambridge which still remains unique in the world. His whole Department was permeated with a wonderful vitality and awareness of what was going on. To work there was to feel the thrill and sense of adventure in penetrating into the secrets of living matter, and life was never dull. We used to look forward to the daily tea in the laboratory, at which Hopkins, sitting at the head of the table, would make interesting and illuminating comments on the latest discoveries. He also presided at the weekly gatherings at which it was (and still is) the custom for one of the members of the Department to present the results of his research—a tradition which has now continued unbroken for more than thirty years. Hopkins' speeches at the annual 'Dunn dinners', at which for an hour or more he used to review the affairs of the Department and poke gentle fun at its members, were always a delight.

Later, when the multiplicity of committee meetings and similar duties made increasing demands on his time, we saw him less often; but the flame which his inspiration had lighted continued to burn, not only in his own Department but also in other centres to which it was carried by many who had worked in his laboratory and come under his influence.

In build, Hopkins appeared slight and even frail, but until his last years he scarcely had a day's illness in the whole of his very active life. He was one of those fortunate people who are practically immune from colds and influenza. Perhaps this freedom from illness made it all the harder to bear when poor health did come upon him a few years before his death. In particular, the loss of his sight while he was still intellectually active was a heavy blow; but he faced it with great courage, and until the year of his death he continued to come to the laboratory almost daily and to carry out interesting research with the aid of E. J. Morgan, his assistant for forty-two years.

Lady Hopkins, whose companionship and care during nearly fifty years of married life contributed greatly to his happiness, survives him. Their son, Dr. Frederick Hopkins, is a physician; their elder daughter, Mrs. Barbara Holmes, is well known as a biochemist, and their younger daughter, Mrs. Jacquetta Hawkes, as an archæologist.

MALCOLM DIXON

No better indication of the deep affection in which Sir Frederick Gowland Hopkins was held by biochemists in general—whether or not fortunate enough to have been his pupils—could be afforded than by the almost universal use among them of his nickname 'Hoppy'. To them he was a dear and lovable character and a great biochemist.

During his long life he saw biochemistry develop from the unfashionable interest of a few distinguished chemists to the stature of the modern science, and in this development he played a major and often decisive part at nearly every stage.

Convinced that an understanding of the processes of life must rest upon a sure knowledge of the structural chemistry of biological materials, his early work was devoted mainly to isolation and characterization. His success with Cole in the isolation from proteins of tryptophane, the indole derivative also being sought by Emil Fischer, gave him particular satisfaction; but in his work on the pterins, those pigments in the wings of white butterflies and which have recently come into such prominence, he was continually hampered by lack of material. As he sadly remarked to me not long ago, he could only make use of what he and friends could collect, whereas Wieland, prosecuting a similar study, could rely upon the proceeds of an organised, nation-wide collection of butterflies by the school-children of Germany.

An investigation of structure alone was to Hopkins a sterile pursuit. The life of the cell is change, "a dynamic equilibrium in a polyphasic system", and it was the duty of biochemistry, he felt, to study and explain the events of metabolism. His isolation of glutathione in 1921 indicated his growing preoccupation with the problem of intra-cellular oxidation, a field which he was so greatly to enrich and to cultivate to the very last. Closely linked with this was the question of the energetics of the cell, the means by which energy set free in the various steps of oxidation was utilized for the performance of vital functions. Hopkins was to see this fundamental problem attacked and developed by his pupils both in Britain and overseas.

The contributions which Hopkins made to nutrition, his careful experiments and the concept of vital accessory factors to which they led, were not divorced

from his other work; they resulted rather from a remarkable development of his biochemical thought, and carry the hallmark of true genius. That proteins, carbohydrates, fats and salts alone are not sufficient to support health and growth was soon apparent—the unknown factors essential but effective in minute amounts could only form parts of the vital intracellular machinery of oxidation and reduction, etc. How clear was this insight has been abundantly proved, and to-day it is accepted as axiomatic that every vitamin will in time be recognized as a constituent of some or other enzyme system.

Hopkins' contributions to his beloved science have been great in the full sense of the word. His unassuming modesty will be equally remembered. To his laboratory came many of the most distinguished men of science; yet to the student or young research worker he was equally available, and each could be assured of a ready and sympathetic understanding of his problems and of advice helpfully and generously given.

Friends, pupils and colleagues have received something from 'Hoppy' which they will cherish throughout their own lifetime. C. RIMINGTON

NEWS and VIEWS

Military College of Science Advisory Council

THE War Office has announced the appointment of an Advisory Council for the Military College of Science under the chairmanship of Sir Henry Tizard (chairman of the Defence Research Policy Committee). The other members are: Prof. J. F. Baker, Sir James Chadwick, Prof. R. A. Peters, Prof. E. K. Rideal, Dr. A. E. Trueman, and Sir Ronald Weeks. Official members are Lieut.-General Sir Sidney C. Kirkman, Dr. O. H. Wansbrough-Jones (scientific adviser to the Army Council), and Lieut.-General F. Wrisberg (Ministry of Supply). The secretary is Mr. E. K. Stopford, Registrar, Military College of Science. The Council thus includes members from the Universities of Oxford, Cambridge and Liverpool, and should therefore be able to ensure that, so far as the special conditions allow, a university atmosphere and the academic traditions of a university are encouraged. The membership of Dr. A. E. Trueman, vice-chairman of the University Grants Committee, provides the link between the Military College of Science and the national structure of university education. The association of the College with the University of London was assured when Prof. C. H. Lander, lately professor of engineering at the Imperial College of Science and Technology, assumed the appointment of Dean of the College.

The new College, which is established in good accommodation at Shrivenham, near Swindon, received its first entry of students in October of last year, and both the number of staff and students is due to increase further. Arrangements have already been made for granting officers attending the College the privilege of sitting as candidates for external degrees in natural and mechanical sciences at the University of London. With the great pressure on all the universities and the urgent necessity of training more men of science, the action being taken by the Army to train its own, without relying on successfully competing for vacancies at the universities, which are urgently needed for young men who intend to make science their career, is to be commended. Provided that high academic standards are aimed at, and the instructional staff are given facilities for research and opportunities comparable to their colleagues in other academic institutions for general scientific intercourse—conditions which are envisaged and which the new Council could doubtless firmly establish—there is every reason why this College should in time take its place within, and make its own definite contribution to, the scientific educational resources of Great Britain. It can only do this in full when it can offer space and facilities to civilian research workers and students—a desirable end which is not likely to be overlooked by this Council. None the less, in the past the Army has gained much, and the universities something, from the practice of sending some young officers to other universities, and it would be unfortunate if, for the future, there were no opportunities for selected Army officers to attend courses elsewhere. The terms of reference of the new Council include the duty of making recommendations on these matters. This experiment and effort which the Army is making to set a higher standard of scientific education among its officers and to discourage the isolationism of military technologists should receive sympathy and encouragement from the academic world in general.

Snowy River Region of Victoria, Australia

THE National Museum of Victoria, Australia, plans to make an ecological survey of the Snowy River area in north-eastern Victoria, and four members of the staff have just returned from a fourteen-day period of preliminary investigation. The area is unknown biologically, and contains some of the roughest and wildest country in the State. With the exception of the Snowy River itself, it has never been surveyed. It is steeply mountainous, with an unbroken series of ranges more than 5,000 ft. high stretching northwards towards Mt. Kosciusko in New South Wales. The country rock of the area is mainly Snowy River porphyry, a massive, coarse-grained, volcanic rock some hundreds of feet thick. The steep mountainsides hold little soil, and there are marked floral differences in the northern and southern aspects. On the northern slopes the country is dry and open; but on many of the southerly slopes, where the sun seldom or never penetrates, comparatively thick 'jungle' exists. General collecting during the preliminary reconnaissance produced some interesting results. The brush-tailed rock wallaby, *Petrogale penicillata* Gray, which for thirty years has been considered extinct in Victoria, was discovered to be still living in small caves and crevices on a tumbled, rocky mountain-side above the Suggan Buggan River. Six species of Phalangeridæ and some native rats were also taken, as were five species of lizards and some interesting frogs. Among invertebrates, several species of land snails (*Charopa*) and a trap-door spider (*Atrax*) are new. Owing to the season (April–May), few insects were on the wing, but interesting species of Coleoptera, belonging to the families Tenebrionidæ, Carabidæ and Paussidæ, were collected, some of which are new to Victoria.

Total Solar Eclipse of May 20 : Preliminary Reports

CONTRARY to all expectation, based on the usual weather conditions in May, the expeditions to the west coast of Africa to observe the total solar eclipse of May 20 were uniformly successful, whereas those to Brazil were upset by cloudy conditions. In Santiago in Chile, conditions were cloudy but observations were made from an aeroplane above the clouds. The corona was reported as of the minimum type with equatorial streamers and polar plumes—an unusual form so near sunspot maximum. At Araxá in Brazil, the Czechoslovak party and the Swedish party under Dr. Öhman were clouded out. At Bocayuva, the Finnish party was able to carry out its time observations for the geodetic programme. The party at the same place from the American Geographical Society, the Georgetown University, Washington, and the Yerkes Observatory reports only partial success owing to clouds. Dr. van Biesbroeck secured plates of the star-field around the sun for the Einstein effect, and photographs of the corona and of its spectrum ; accurate time observations of the contacts were obtained. Photographs were taken from an A.A.F. *B* 17 plane flying at 30,000 ft. ; also a programme of ionospheric observations was successfully carried through.

In West Africa, both the Finnish and the Swedish expeditions were favoured by clear weather and were able to carry through their cinematograph programme for the determination of the contacts, on the scheme drawn up by Bonsdorff. The Swedish expedition under Dr. B. Aurell recorded cinematographically the crescent as well as the flash spectrum. The American party at Bocayuva also reports that, while there, long-exposure photographs of the southern Milky Way were taken and measurements made of the intensity of cosmic rays.

A Solar Variation of 6·6456 Days ?

DR. C. A. ABBOT, in *Smithsonian Miscellaneous Collections*, Vol. 107, No. 4, announces that "there is a regular period of 6·6456 days in solar variation, and that terrestrial temperatures respond with changes ranging from 2° to 20° F. in exactly the same average period of recurrence. While the sun's variation appears to be perfectly regular in phase, always recurring on the day predicted, the terrestrial responses come sometimes for a month or more in succession from 1 to 3 days early or late. This, which by mechanical analogy we might call backlash, is doubtless the circumstance which hitherto has prevented meteorologists from recognizing the nature of this large temperature variation." It is to be feared that "meteorologists, physicists and astronomers" who, as Dr. Abbot remarks, "with few exceptions, have remained to this day skeptical as to whether the Smithsonian observations of the solar constant really discover solar variations from day to day", will manifest the same attitude to this new announcement. It is greatly to be regretted that Dr. Abbot, who has done so much to promote our knowledge of the solar 'constant', should so persistently refrain from using standard statistical methods for the discussion of his data, and proper statistical criteria for testing the significance of his results. The use of the word 'period' in connexion with an interval given to five significant figures (or 0·0001 day), when its phase is liable to be from one to three days too early or late, will generally be regarded as inappropriate, and neither the temperatures nor the solar data appear to warrant this pretention to accuracy in the period. The amplitude of the variation in both sets of data changes irregularly from one 'period' to the next, the average range in the solar variation being 0·13 per cent of the solar constant. The discussion is commendably sensible in its claims as to the practical value of this work for meteorological prediction.

National Central Library

THE thirtieth annual report of the National Central Library, covering the year ended February 28, 1946, refers to a gradually growing demand on the central stock of the Library, and on the resources of the regional library systems, university and 'outlier' libraries. Although most of the members of the staff absent on national service have now returned to the Library and new appointments have been made, the personnel has not yet been brought up to the 1939 level. The task of administration has been lightened, however, by the return from Bourne End of all the bibliographical apparatus, the union catalogues and the Library of Congress catalogue, and other material of the Bureau of American Bibliography. These are now at Woburn Square, London, and the transfer includes also the union catalogue, records and staff of the South-Eastern Regional Bureau. Among the more urgent tasks of the Library is the replenishment of the stock of the more specialized and valuable books which were lost by enemy action in 1941, and it has been arranged that the Library, next in order after the British Museum, shall select from the Inter-Allied Book Centre such books as are suitable to replace part of its losses. Another urgent task is the overtaking of large arrears of cataloguing of books which have come into the Library from various sources in recent years, and of much larger arrears of editing and incorporating entries into the national union catalogue and the union catalogue of outlier libraries, and of removing entries for books withdrawn. The executive committee has approved a request made by the executive sub-committee of the Foreign Office Committee on Russian Studies that the Library should undertake the compilation of a union catalogue of books in the Russian language in libraries in the United Kingdom.

Total issues of books from or through the Library during the year were 59,671 as against 57,672 in 1944–45. Included in this total are 5,369 volumes to university libraries as against 3,538 in 1938–39, while issues to libraries of Government departments, research and industrial organisations, etc., were 7,465 as against 2,588 in 1938–39. Issues from the Scottish and Irish Central Libraries were 12,412 and 13,651 respectively, while 10,701 volumes were issued from the Adult Class Department. 'Outlier libraries', of which a list is given in the report, lent 8,512 books as against 11,361 in 1938–39, and 88,728 books were lent by the regional library systems in England, Wales and Scotland.

A.W.A. Technical Review

FOR several years past, some of the progress made by Australian workers in the field of radio-frequency technique has been recorded in the *A.W.A. Technical Review*, published by Amalgamated Wireless (Australasia), Ltd., in Sydney. The first number of volume 7 (September 1946) of this publication contains several papers of interest, some of them describing measuring equipment developed by the above

organisation. A resistance-capacitance beat-frequency oscillator covering the range 0–5,000 cycles per second is described by D. S. Robertson and L. C. Nye, certain features underlying the design having been developed theoretically in another paper by L. E. V. Lynch and D. S. Robertson. A description is also given by L. G. Alexander of an equal-ratio impedance bridge by means of which impedances can be measured to a precision of 1 per cent or better at frequencies up to 3 Mc./s.; while two special-purpose receivers covering the range of frequencies from 50 kc./s. to 50 Mc./s. are described by B. Sandel. In a paper entitled "Directional Patterns of Rhombic Antennæ", W. N. Christiansen examines the spatial radiation patterns of typical rhombic antennæ in relation to that of a large tuned array, to which a single rhombic is inferior. After discussing various simple designs, the author shows that it is possible to arrange several rhombics in the form of an interlaced 'end-on' array so as to produce over the whole frequency range of the rhombic aerials a directional radiation characteristic which compares well with that of a tuned array at its single designed frequency. Other papers in this issue deal with such subjects as the application of a Geiger counter for determining the thorium content in wire used in valve manufacture, a radio-frequency form of high-tension supply for cathode-ray tubes, and a vacuum-sealed relay designed for operation with aircraft aerials transmitting at high voltages.

Bacteriology in the Kitchen

An interesting article by Dr. Irene Hutchinson (*Brit. Med. J.*, 134, Jan. 25, 1947) directs attention to the unsatisfactory methods employed in many communal feeding centres for the cleaning of utensils used for eating. In a London dormitory town in which food inspection was kept at a very high level, unannounced visits were made to twenty-five kitchens of hotels, restaurants of multiple stores, day-nursery kitchens, teashops, snack bars and a civic restaurant. Samples of washing-up water in actual use were taken at the peak hour between 12.30 and 1.30 p.m., when conditions were at their worst, and swabs were taken from spoons, cups, forks, glasses and plates which had been used and washed and were ready to be used again. The organisms obtained from these sources are listed, and Dr. Hutchinson concludes that the cleaning of eating utensils is "very unsatisfactory, and that pathogenic organisms are likely to be spread by the users of different articles". The lack of washing machines, the difficulty of getting soap and washing powders and the scarcity of drying towels make it very difficult to feed people hygienically. In one only of the twenty-five kitchens were dysentery bacilli found on spoons, and Dr. Hutchinson comments that this "may suggest the origin of the sporadic case of 'diarrhœa'". Other findings of pathogenic staphylococci may help to explain the high incidence of septic mouth lesions so common during recent years. The proprietors of the various premises visited showed great interest in the work and helped it in every way that they could. An annotation in the same issue of the *British Medical Journal* (p. 143) critically discusses the results obtained, and suggests that the greatest need is for education of the people who handle food. In the United States much progress has been made in this matter, and in Great Britain the Central Council for Health Education is arranging courses of instruction on food hygiene for food handlers (*Health Educ. J.*, January, 1947, p. 11). Facilities for dish-washing and for the cold storage of food, says the annotation, need to be greatly improved. Few people will disagree with this conclusion. It may be compared with the need for the adequate treatment and care of milk bottles which was discussed in *Nature* (153, 31; 1944).

Agriculture in Malaya

After a break of five years, the *Malayan Agricultural Journal* has reappeared, though for 1947 it will be published as a quarterly only. Vol. 30, No. 1, contains a message from the governor of the Malayan Union, Sir Edward Gent, and a foreword from the Director of Agriculture. The Department was fortunate in being able to resume active work through its field branch shortly after the liberation of Malaya, the staff being now almost back to pre-war strength. Food production and general rehabilitation have been its chief immediate concern, but long-range plans are already under consideration. These include the establishment of a Central Government Fruit Experiment Station, the rehabilitation of rubber smallholdings of high-yielding clonal material, canning and food preservation, the expansion of the School of Agriculture at Serdang, and development of the livestock industry. Among the original articles in this number is an account of intensive gardening in a prisoner-of-war camp which cannot fail to be of interest to all readers.

'Positex'

An 8-page pamphlet, 'Positex' Pamphlet No. 2, published by the British Rubber Development Board, 19 Fenchurch Street, E.C.3, and written by Dr. C. M. Blow, deals with the compounding, pigmenting and thickening of 'Positex', a form of rubber latex in which the particles carry a reversed or positive charge. There are also some notes on the removal of rubber from fibrous materials. The research work referred to in the pamphlet was carried out by the Wool Industries Research Association, in collaboration with the Technical Research and Development of New Uses Committee of the Rubber Growers' Association, and later with the British Rubber Producers' Research Association. The introductory pamphlet to the series gave a general account of the material and of its possible commercial applications. Licensees for 'Positex' in Great Britain are Messrs. Revertex, Ltd., King William Street House, Arthur Street, London, E.C.4, and Messrs. Veedip, Ltd., St. Helens Works, Slough.

Engineering Degree Courses for Ex-Servicemen

Mr. O. S. Puckle, of R. F. Equipment, Ltd., Langley Park, Nr. Slough, Bucks, recently invited inquiries from engineers and others wishing to study for science and engineering degrees (*Nature*, April 12, p. 497). He now states that he has received a total to date of ninety-three completed questionnaires. Of these, fifty-one are from the London area, including Dartford and south-west Essex, and ten from Stoke-on-Trent. The numbers in each of the other localities are too small to make it possible to ask the Ministry of Education to take action; but it is hoped that in London and Stoke it may be possible to arrange the suggested courses. He is communicating with the Ministry of Education, to whom the questionnaires and an analysis of the results are being sent. Those who have not yet returned the questionnaires for

which they asked should do so immediately, especially if they wish to take courses in the London area or in Stoke.

Conference on Infestation of Stored Foodstuffs

THE Food and Agriculture Organisation of the United Nations has invited its forty-seven member Governments to send experts to meet in London during August 5–12, for a conference on the problems of infestation of stored foodstuffs. This term includes food undergoing transit, storage and processing. Problems to be studied include measures to prevent infestation such as adequate improved warehousing facilities, as well as a study of methods of pest control used in the various countries. Also to be investigated are world foci of infestation and the channels through which insects, mites, rodents and mould fungi are carried in foodstuffs to all parts of the world. Aspects of the production, availability, and consumption of insecticides, fungicides, fumigants and rodent poisons will also be examined. An attempt will be made to obtain some idea of the extent of the very grave losses which are known to occur through infestation, and to recommend measures which could be applied to prevent these losses. A report of the recommendations of the meetings will be submitted by the Food and Agriculture Organisation to all member Governments and to other interested international agencies.

Congress of the Universities of the British Empire

IT is announced that, at the invitation of the University of Oxford, the next Congress of the Universities of the Empire will be held in Oxford during July 19–23, 1948. The Universities Bureau of the British Empire is requesting each of its member institutions to appoint four delegates, and although present conditions have necessitated this limitation of numbers, it is expected that about three hundred senior teaching and administrative officers will attend as representatives of universities and other institutions of higher learning, both home and overseas. The subjects for discussion at the various sessions will be announced later.

There have been five previous congresses, the first having been held in London in 1912 as the result of a resolution adopted by the Senate of the University of London in 1909. All the universities of the Empire sent delegates to that meeting, when it was agreed to establish the Universities Bureau in London and to hold congresses regularly every five years for the discussion of questions of academic policy of common interest. The two World Wars have interrupted this quinquennial programme of meetings; but congresses were held in 1921 (at Oxford), 1926 (at Cambridge), 1931 (at Edinburgh), and 1936 (at Cambridge). The 1948 gathering will therefore be the first general meeting for twelve years of official representatives of the universities of the British Commonwealth and Empire.

University of Glasgow: Chair of Physiological Chemistry

PROF. JAMES NORMAN DAVIDSON has been appointed to the Gardiner chair of physiological chemistry in succession to Prof. G. M. Wishart. Prof. Davidson graduated in chemistry at Edinburgh in 1934, and later took the degrees of M.D. (1939) and D.Sc. (1945). During 1937–38 he worked with Warburg at the Kaiser Wilhelm Institute for Cell Physiology. He has held lectureships in biochemistry at Dundee and St. Andrews; has been on the scientific staff of the Medical Research Council; and for the past year has been professor of biochemistry at St. Thomas' Hospital Medical School, London (see *Nature*, **157**, 760; 1946). His research work touches on many fields, including those of carbohydrate metabolism and of the nucleic acids.

Announcements

SIR ALEXANDER FLEMING and Sir Howard Florey have each been awarded the Gold Medal of the Royal Society of Medicine for their work on penicillin. The Medal is normally given once in three years, but on this occasion two were awarded.

DR. JOHN H. LAWRENCE, of the University of California, will deliver the twenty-fourth Mackenzie Davidson Memorial Lecture at the British Institute of Radiology on July 17, at 8 p.m., in the Reid-Knox Hall, 32 Welbeck Street, W.1. He will speak on "The Application of Artificial Radioactivity to Biology and Medicine".

MR. HAROLD CLAUGHTON is retiring from the post of principal of the University of London on December 31, and the Senate, with the concurrence of the Court, has appointed Dr. D. W. Logan, clerk of the University Court since 1944, to succeed him.

AT the University of Aberdeen on July 3 the honorary degree of LL.D. was conferred on Prof. C. D. Broad, Knightsbridge professor of moral philosophy in the University of Cambridge. Among other degrees conferred was that of Ph.D. on K. Hassan for a thesis on "Factors affecting the Utilization of Phosphorus in the form of Phytic Acid by the Ruminants"; and M.D. on L. D. M. Gavin for a thesis on "The Military Malaria Campaign in Greece, 1945".

THE following elections to the Paris Academy of Sciences have been announced: M. Pierre Teilhard de Chardin, Gaston Delépine, of Lille, and Prof. Pierre Pruvost, professor of geology and mineralogy in the University of Lille, *correspondants* for the Section of Mineralogy; Prof. H. A. Kramers, professor of mathematical physics in the University of Leyden, and Prof. René de Mallemann, professor of physics in the University of Nancy, *correspondants* for the Section of General Physics; Prof. Emile Briner, professor of theoretical and technical chemistry in the University of Geneva, Dr. C. H. Desch, honorary scientific adviser to the Iron and Steel Research Council, and Prof. Hans von Euler, professor of chemistry in the Stockholms Högskola, *correspondants* for the Section of Chemistry.

MR. G. F. COLE, who for the past year has acted as assistant secretary of the Illuminating Engineering Society, has now been appointed secretary of the Society.

THE following appointments have been made in the Colonial Service: A. B. Cahusac, assistant conservator of forests, Uganda; M. S. Philip, assistant conservator of forests, Uganda; A. C. M. McKinlay, geologist, Tanganyika Territory; R. K. J. Gascoigne (agricultural officer, Nigeria), entomologist, East African Anti-Locust Directorate, Kenya.

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications

Constitution of the Succinate and α-Glycerophosphate Oxidase Systems

THE succinate and glycerophosphate dehydrogenases belong to the group of 'cytochrome-reducing dehydrogenases'[1]. In some tissues the succinic system is by far the more active, but in others (for example, rabbit skeletal muscle) the two systems are equally important. Hopkins *et al.*[2] suggested that in the succinoxidase system from heart muscle there was an intermediate factor linking the dehydrogenase with cytochrome *c*. Stern and Melnick[3] claimed to have separated the factor, although their evidence has been rightly questioned[4]. Straub[5] has shown that an oxidase preparation lacking the factor can be reactivated by a heart-muscle dispersion in which the succinic dehydrogenase and cytochrome oxidase have been destroyed. Experiments reported below show the existence in liver of a *soluble* factor which links or makes accessible the succinodehydrogenase to the cytochrome system. This factor or activator is not necessary for the α-glycerophosphate system.

The method of preparation is as follows: 250 gm. chopped ox or rabbit liver are minced in a Waring blendor for 3 min. with 500 ml. of 0·02 *M* disodium hydrogen phosphate; the suspension is centrifuged for 30 min. at 3,000 r.p.m., and the precipitate again extracted for 1 min. with 400 ml. of 0·02 *M* disodium hydrogen phosphate in the blendor and centrifuged. The united extracts are diluted to 1·2 l. with distilled water, ammonium sulphate added to 0·20 saturation, and left 12 hours at 0°. The precipitate formed is centrifuged off, washed with 400 ml. of cold 0·20-saturated ammonium sulphate, taken up in distilled water, dialysed in the cold until free from ammonium sulphate, and brought to *M*/15 with phosphate buffer *p*H 7·4 ('enzyme preparation'). The supernatant liquid is made 0·33 saturated with ammonium sulphate, left 6 hours at 0°, centrifuged, and the clear red supernatant liquid brought to 0·50 saturation with ammonium sulphate. The precipitate now formed is filtered in the cold, dissolved in 400 ml. distilled water, and dialysed for 12 hours at 0° (the slight precipitate of denatured proteins is spun off). The dialysed solution is adsorbed with three successive portions of 50 ml. calcium phosphate gel (36 mgm./ml.), the gel centrifuged and eluted with four successive portions of 20-ml. 0·2 *M* disodium hydrogen phosphate, the water-clear eluate dialysed and neutralized if necessary ('factor preparation').

The accompanying illustration shows the aerobic oxidation of succinate by the system. Although the enzyme preparation contains active succinodehydrogenase and cytochrome oxidase, the oxidation is slow, even with added cytochrome *c*. Addition of the activator, however, produces a rapid oxidation, which is dependent on the presence of cytochrome *c*.

TABLE 1

Test for	Reactants	Q_{O_2} given by Enzyme	Factor	Enzyme +factor
Succinodehydrogenase:	Succ. +ferricyanide	22·0	0·0	20·0
Succinoxidase:	Succ. +cyt. *c* +O_2	9·5	0·0	44·8
Succinoxidase:	Succ. +O_2	0·0	0·0	0·1
Cytochrome oxidase:	*p*-phenylenediamine +cyt. *c* +O_2	49·5	0·0	48·0

Initial concentrations: sodium succinate 0·01 *M*; cytochrome *c* 0·5 × 10^{-4} *M*.; $K_3Fe(CN)_6$ 0·8 per cent; *p*-phenylenediamine 0·01 *M*. For ferricyanide method, bicarbonate buffer 0·02 *M* with 5 per cent carbon dioxide in nitrogen; for oxygen uptakes, *p*H 8·0 phosphate buffer *M*/15 with air. Barcroft manometers, temp. 38°.

Table 1 shows the succinodehydrogenase, succinoxidase and cytochrome oxidase activities of the preparations, expressed in Q_{O_2}. The dehydrogenase could not be determined by the usual methylene blue technique, as the dye, like cytochrome, is only slowly reduced without the factor. The ferricyanide technique[6] was satisfactory and was not affected by the factor. In calculating the Q_{O_2}, 4 mol. of ferricyanide were taken as equivalent to 1 mol. of oxygen. The cytochrome oxidase was measured as usual by the oxidation of *p*-phenylenediamine, which again was not affected by the factor.

The factor loses its activity on heating to 70° for 10 min. or on exposure to *p*H 4·6 for 60 min. It cannot be replaced by diaphorase, malic dehydrogenase, fumarase, catalase, flavin dinucleotide, riboflavin, calcium and/or aluminium ions [10^{-5} *M*], cysteine or glutathione.

A rabbit skeletal muscle preparation in which the factor has been inactivated by treatment at *p*H 4·6 for 60 min., and which has therefore lost its succinoxidase activity, is still able to oxidize α-glycerophosphate in presence of ferricyanide or cytochrome *c* with about the same velocity, as shown in Table 2.

TABLE 2

Reactants	Q_{O_2} given by Acid-treated	Normal
Succ. +cyt. *c* +O_2	0·2	21·0
Succ. +ferricyanide	6·8	16·2
p-Phenylenediamine +cyt. *c* +O_2	16·0	25·0
α-Glycerophosphate +cyt. *c* +O_2	15·5	24·0
α-Glycerophosphate +ferricyanide	16·0	24·5

Initial concentrations: sodium α-glycerophosphate 0·01 *M*; others as for Table 1.

I should like to thank Dr. M. Dixon for suggestions and for his interest in the work.

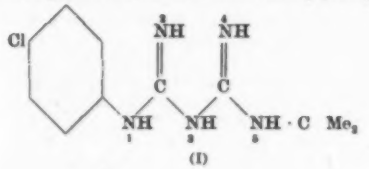
A. O. M. Stoppani

Biochemical Laboratory,
Cambridge.
April 21.

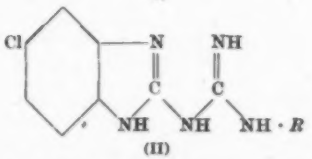
[1] Green, D. E., and Brosteaux, J., *Biochem. J.*, **30**, 1489 (1936).
[2] Hopkins, F. G., Lutwak-Mann, C., and Morgan, E. J., *Nature*, **143**, 556 (1939).
[3] Stern, K. G., and Melnick, J. L., *Nature*, **144**, 330 (1939).
[4] Keilin, D., and Hartree, E. F., *Proc. Roy. Soc.*, B, **129**, 277 (1940).
[5] Straub, F. B., *Z. physiol. Chem.*, **272**, 219 (1941).
[6] Quastel, J. H., and Wheatley, A. H. M., *Biochem. J.*, **32**, 936 (1938).

Benziminazoles Related to Paludrine

The suggestion recently made in these columns by Hawking[1], that the drug paludrine is not itself an antimalarial agent but is converted into an active compound *in vivo*, opens up a wide field for speculation and research. No indication has yet been obtained as to the nature of this transformation product; but one of the more obvious hypotheses as to the fate of paludrine in the body appears to be excluded by an investigation which we have lately completed.



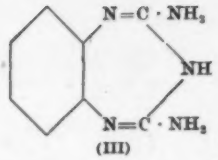
(I)



(II)

Consideration of the paludrine molecule (I) in the form of a model shows that, without introducing any appreciable strain, it is possible for N^3 to approach the benzene ring and by the loss of two hydrogen atoms to form a new bond. Should this oxidation be a step in the metabolism of paludrine, then the related guanidinobenziminazole (II, $R = CHMe_2$) would be expected to show comparable biological activity. Bearing in mind that the growth of certain micro-organisms can be inhibited by benziminazole, which interferes with the utilization of guanine and adenine[2], paludrine would thus appear to function as an antagonist of some specific purine essential to the malaria parasite.

The benziminazole (II, $R = CHMe_2$), which we accordingly synthesized, has many of the chemical properties of paludrine, as might be expected from the very close resemblance of the two structures. For example, it is readily converted into a chelate copper derivative, a reaction implying the formation of a dimolecular complex similar in outline to the porphyrin ring-system. It has been suggested by Curd and Rose[3] that it is this characteristic which may be connected with the antimalarial action of paludrine. It is remarkable, therefore, that the guanidinobenziminazole (II, $R = CHMe_2$) and several analogous benziminazoles, none of which is more toxic than the antimalarial, are, at the maximum tolerated dose, without action on *P. gallinaceum* infection in chicks.



(III)

The benziminazoles with unsubstituted guanidino side-chains, for example (II, $R = H$), were synthesized from *o*-phenylenediamines and dicyandiamide[4]. The N^3-*iso*propyl derivatives, for example (II, $R = CHMe_2$), were obtained similarly from the *iso*propyl dicyandiamide, which was prepared from dicyanimide and *iso*propylamine. An attempt to carry out the synthesis of N^3-*iso*propylguanidinobenziminazole in the reverse direction, starting with *o*-phenylenediamine and dicyanimide, led to the formation of a seven-ring compound, 2 : 4-diamino-1 : 3 : 5-triazabenzepine (III), a structure comparable with that obtained from *o*-phenylenediamine and malonic acid[5].

A full account of this work will be published in due course. The biological experiments were kindly carried out by Mrs. A. M. Yates, of the National Institute of Medical Research, London, N.W.3.

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F. E. King
P. C. Spensley

Dyson Perrins Laboratory,
Oxford.
April 19.

[1] Hawking, *Nature*, **159**, 409 (1947).
[2] Woolley, *J. Biol. Chem.*, **152**, 225 (1944).
[3] Curd and Rose, *Nature*, **158**, 707 (1946).
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[5] Phillips, *J. Amer. Chem. Soc.*, **64**, 187 (1942).

Urinary Excretion of Phosphate with $^{32}_{15}P$ as Indicator

The phosphate excretion by the kidney follows different laws well determined by L. Brull[1] and since confirmed by other investigators. However, the mechanism of the excretion of phosphate has not been completely explained. Thus it was considered of interest to study the mechanism of excretion of phosphate by the kidney, using radiophosphorus $^{32}_{15}P$. (The $^{32}_{15}P$ was prepared by Dr. F. A. Heyn (Philips, Eindhoven), and I am indebted to him for his co-operation and generosity.)

Dogs are anæsthetized by chloralose, the ureters are catheterized and small samples of urine are collected. Blood samples are taken from the femoral artery. The dogs received intravenously labelled disodium phosphate solutions containing about 1–100 mgm. phosphorus. The radioactivity of the samples of urine and blood are measured as well as the total phosphorus content.

The table shows the data obtained in one experiment. The dog weighed 4 kgm. and received 97·13 mgm. labelled phosphorus in five minutes. Fig. 1 shows the excretion of total and exogenous phosphorus in the urine. The variation of percentage exogenous phosphorus present in total phosphorus of the plasma and the urine during the experiment is shown in Fig. 2. The number of animals used was thirty.

From Figs. 1 and 2 it can be seen that after phosphate injection the inorganic phosphate of the urine, at least in the first samples, contains more than 90 per cent exogenous phosphate, while the level of the

PLASMA

Time	Total P in 100 c.c. (mgm.)	Per cent radio P in 100 c.c.	Exogenous P in 100 c.c. (mgm.)	Per cent exogenous P in total P
0	4·14	—	—	—
8	18·00	13·17	12·79	71·0
12	15·12	10·34	10·05	69·5
17	12·12	4·68	4·54	37·5
25·5	10·41	3·97	3·85	37·0
45·5	8·70	2·46	2·39	27·5
81	9·60	1·64	1·60	16·6

URINE

Time	Urine (c.c.)	Total P per min. (mgm.)	Per cent radio P per min.	Exogenous P per min. (mgm.)	Per cent exogenous P in total P
6	2·3	0·031	—	—	—
9	1·8	1·134	1·123	1·091	96·2
12·5	1·5	1·440	1·145	1·410	97·9
17·5	1·5	0·748	0·674	0·655	87·5
23·5	1·6	0·570	0·334	0·324	57·0
30	1·5	0·401	0·211	0·205	51·1
42	1·9	0·293	0·118	0·114	39·1
57	1·2	0·118	0·030	0·029	24·6
84	3·9	0·099	0·023	0·022	22·6

latter in the plasma is distinctly lower. Only a very small part of endogenous phosphate is present in the urine during the first minutes following the injection. Later on, the exogenous phosphate in the urine decreases, and after about 1¼ hr. it is nearly equally distributed between the plasma phosphate and the urine inorganic phosphate. Similar results were obtained by injection of small quantities of phosphate (1–2 mgm. phosphorus), which do not modify the level of phosphate in the plasma.

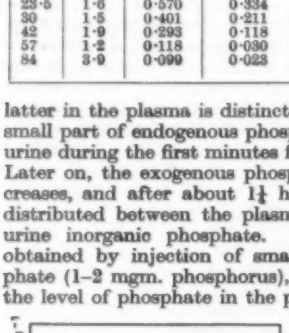

Fig. 1

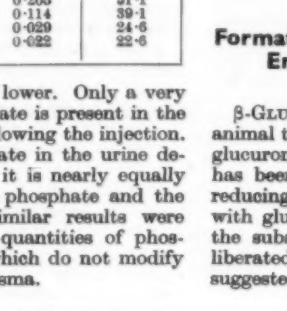

Fig. 2

The kidney must be considered as a very sensitive test organ, since it distinguishes between constituents which chemical methods are unable to separate. Exogenous phosphate is handled differently from endogenous phosphate by the kidney. The injected phosphate, in a pure inorganic form, is excreted by the kidney at much higher speed than normal plasma phosphate. We may conclude that an important fraction of the so-called inorganic phosphate in the plasma is in a different physico-chemical state from that of the injected phosphate. Only a small fraction of the acid-soluble phosphate is in a pure inorganic form, and I suggest calling the other fraction 'phosphate-X'.

After 1¼ hr., the percentage of exogenous phosphate being nearly the same in plasma and urine, we may admit the existence of an exchange of phosphate between the pure inorganic phosphate and phosphate-X. This exchange does not occur *in vitro*; exogenous phosphate appears chiefly in the urine also when labelled blood is administered. Such blood is obtained by preserving at 37° for 3 hr. a mixture of blood with a solution of labelled phosphate.

The renal threshold for phosphate, which is governed by certain renal factors (parathyroid), also depends upon the physico-chemical state of phosphates in the plasma. Probably the small fraction of pure inorganic phosphate of the plasma is responsible for the urinary phosphate.

I wish to express my thanks to Prof. L. Brull for much assistance.

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Laboratoire de Radioactivité
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University of Liège.
March 18.

[1] Brull, L., *C.R. Soc. Biol.*, **98**, 325 (1928); **99**, 1605 (1928). *Arch. Intern. Physiol.*, **32**, 138 (1930); *Ann. Physiol.*, **12**, 635 (1936).

Formation of Glucuronic Acid during the Enzymic Hydrolysis of Conjugated Glucuronides

β-GLUCURONIDASE, an enzyme found in many animal tissues, catalyses the hydrolysis of conjugated glucuronides *in vitro*. The activity of preparations has been determined by measuring the increase in reducing power which occurs when they are incubated with glucuronides, the assumption being made that the substance causing reduction is glucuronic acid liberated during the hydrolysis[1–3]. It has been suggested[4,5] that the synthesis of glucuronides *in vivo* proceeds by a reversal of the hydrolysis observed with this enzyme *in vitro*. Lipschitz and Beuding[4] found, however, that the synthesis of glucuronides by liver slices is stimulated, not by glucuronic acid, but by certain C_2 compounds. By the method of Lohmar *et al.*[7], the presence of *d*-glucuronic acid in the residue from hydrolysis of a glucuronide with β-glucuronidase has been demonstrated, suggesting that this enzyme is distinct from the system causing synthesis in Lipschitz and Beuding's experiments. A brief description of the experimental procedure follows. Fuller details will be published elsewhere.

To 700 mgm. of biosynthetic *dl*-menthol glucuronide[8] in 10 ml. 0·4 *N* acetate buffer at *p*H 5 was added 10 ml. of a purified preparation of β-glucuronidase from beef spleen[3], containing 500 'glucuronidase units'[3]. The mixture was kept at 37° for 24 hours and then dialysed at 0° against 80 ml. water for a further 24 hours. After the addition of 2 ml. 11 *N* sulphuric acid to the dialysate, menthol and unreacted menthol glucuronide were removed by extraction with ether. The aqueous layer was shaken vigorously with solid barium carbonate to neutralize the acid and precipitate sulphate ion, and filtered. The *p*H of the filtrate, originally about 7·5, was brought to 7, and water removed *in vacuo*. From determinations carried out on a very small fraction[9], it appeared that the reducing power of the whole residue was equivalent to 148 mgm. glucuronic acid. After oxidation, the residue yielded 60 mgm. of the dibenziminazole derivative of the corresponding saccharic acid, m.p. 234–35°. Control experiments showed no liberation of glucuronic acid in the absence of enzyme under the conditions of the experiment.

	Substance isolated	Authentic specimen	Mixture
Dibenziminazole Dihydrochloride tetrahydrate	m.p. 243° m.p. 265° $[\alpha]_D^{18°} = +52·3°$	m.p. 240–2° m.p. 267° $[\alpha]_D^{18°} = +52·3°$	m.p. 240° m.p. 265–6°
Diplcrate trihydrate	Change of form 145°; m.p. 211°	Change of form 145°; m.p. 211°	Change of form 140°; m.p. 211°

All melting points corrected. Decomposition before or at m.p. in every case.

The experiment was repeated using only 300 units of enzyme, but continuing incubation for 48 hours. The residue from the hydrolysis appeared to contain 195 mgm. glucuronic acid, and gave 105 mgm. of the iminazole, m.p. 235–36°. This was combined with the product of the first experiment and put through one stage of purification, giving a final yield of 130 mgm. The hydrochloride and picrate were prepared, and as shown by the data in the table the identity of the iminazole with an authentic specimen prepared from *d*-glucosaccharic acid was proved.

G. A. Levvy

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April 14.

[1] Masamune, H., *J. Biochem. Japan*, **19**, 353 (1934).
[2] Fishman, W. H., *J. Biol. Chem.*, **127**, 367 (1939).
[3] Graham, A. F., *Biochem. J.*, **40**, 603 (1946).
[4] Fishman, W. H., *J. Biol. Chem.*, **136**, 229 (1940).
[5] Fishman, W. H., and Fishman, L. W., *J. Biol. Chem.*, **152**, 487 (1944).
[6] Lipschitz, E., and Beuding, W. L., *J. Biol. Chem.*, **129**, 333 (1939).
[7] Lohmar, R., Dimler, R. J., Moore, S., and Link, K. P., *J. Biol. Chem.*, **143**, 551 (1942).
[8] Williams, R. T., *Biochem. J.*, **32**, 1849 (1938).
[9] Levvy, G. A., *Biochem. J.*, **40**, 396 (1946).

Assay of Cation-Active Antiseptics

The agar-plate or the cylinder-plate method of testing the effectiveness of antiseptics and antibiotics is now a well-known laboratory technique; and it is the basis of quantitative estimations of penicillin and of other antiseptics. There is little doubt that the degree of 'zoning' obtained is an excellent criterion of a good chemotherapeutic agent, and Fleming[1] considers that this test should be so applied. However, recent experiences in my laboratory indicate that this test is not necessarily a good criterion for cation-active antiseptics of the class of quaternary ammonium salts, such as cetyl trimethyl ammonium bromide ('Cetavlon') and cetyl pyridinium chloride ('Ceepryn').

Solutions of 1/1,000 of the latter compound and of the corresponding bromide, which have been shown to be bactericidal to many organisms (such as *Staph. aureus*) in dilutions of 1/50,000 *in vitro* give very little zoning by the agar cylinder-plate method, and, in the form of creams, by the agar-plate method. Creams containing other antiseptics (such as potassium hydroxy quinoline sulphate) give, in the correct concentrations, large zones; but there seems to be no great advantage in the use of these creams clinically as compared with creams made from cetyl pyridinium bromide.

A possible explanation of this may be found in the different chemical constitution of the cation-active antiseptic and the quinoline compound, although both are sufficiently water-soluble. It is possible that the ionic aggregates of the cetyl pyridinium ion are physically too large to pass through the agar network, and that this does not apply to the physically smaller molecules of the hydroxy quinoline compound. Since wound exudate or the surface moisture of the skin is not a network, the cation-active antiseptic is able to penetrate it as freely as is necessary to exert its bactericidal activity.

It seems from this that although the agar methods are suitable for testing many ointments and creams, it may not be the most suitable for testing creams (or solutions) based on cation-active materials; for such creams, the inoculation tests would appear to be preferable. Indeed, preliminary tests by this method with creams containing cetyl pyridinium chloride and bromide are much closer parallels to the clinical findings than those tests performed by the agar methods.

I have been informed by Sir Alexander Fleming (private communication) that he found some years ago that antiseptics of the quaternary ammonium salt type did not diffuse into agar, which is a property he considers to be very important; but it seems that these observations, confirmed in my laboratory in the case of cetyl pyridinium bromide and chloride, have not hitherto been published.

The pharmacological and clinical results will be published as soon as complete.

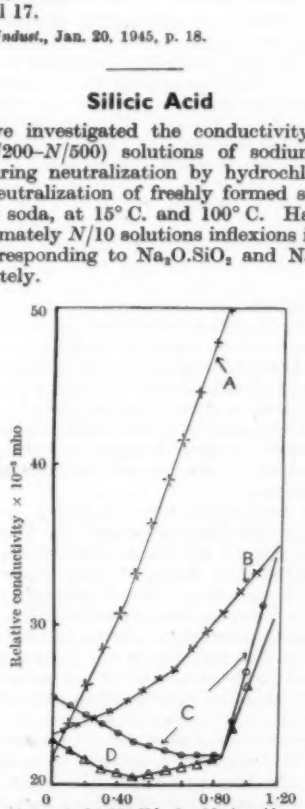
M. A. Phillips

7 Harley Street,
London, W.1.
April 17.

[1] *Chem. and Indust.*, Jan. 20, 1945, p. 18.

Silicic Acid

We have investigated the conductivity of very dilute ($N/200$–$N/500$) solutions of sodium normal silicate during neutralization by hydrochloric acid, and the neutralization of freshly formed silicic acid by caustic soda, at 15° C. and 100° C. Hagg found in approximately $N/10$ solutions inflexions in the *p*H curves corresponding to $Na_2O.SiO_2$ and $Na_2O.2SiO_2$ approximately.



A: 500 c.c. $N/500$ H_2SiO_3 at 100° C.
B: 200 c.c. $N/200$ H_2SiO_3 at 15° C.
C: 500 c.c. $N/500$ Na_2SiO_3 at 100° C.
D: 200 c.c. $N/200$ Na_2SiO_3 at 15° C.

With very dilute solutions at room temperature, three sharp breaks occur in the conductivity curve for the neutralization of Na_2SiO_3 with hydrochloric acid, suggesting the presence of ions from $Na_4Si_2O_8$, $NaHSiO_3$ at the termination of the respective stages. Titration of silicic acid freshly liberated from Na_2SiO_3 with sodium hydroxide at room temperature gave only two breaks. The first corresponded to $2Na_2O3SiO_2$, the second to Na_2O2SiO_2.

When the measurements were made at the boiling point of water, the form of both curves changed considerably. Sodium silicate showed $Na_2O.2SiO_2$ and $Na_2O.4SiO_2$, while boiling very dilute silicic acid showed only evidence of $Na_2O.2SiO_2$.

The observations were made with a Wien A.C. bridge, and the breaks in the conductivity curves increased in sharpness as the dilution increased. The solutions of sodium silicate were made immediately in cold water from Merck's Natrium silicium purum cryst. in $N/2$ solution in water, which analysis showed was ($Na_2O.SiO_2$) with water of crystallization.

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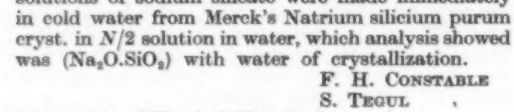
University of Istanbul.

Co-ordinate Bond Formation by Olefins

It is pertinent to add to Dr. Walsh's remarks[1] concerning co-ordinate bond formation by ethylene analogous to that commonly associated with formally saturated molecules possessing lone electron pairs that an essentially similar point of view was first presented by Winstein and Lucas[2]. These authors visualized the olefin-electron acceptor (X) complex as a resonance hybrid involving the structures I, II and III:



(I) (II) (III)

and recognized the significance of this bonding to a wide range of olefinic reactivity. I pointed out the application of this concept to the aromatic hydrocarbon-polynitro compound addition complexes, using simple olefin complexes such as Reise's salt as illustration, at a meeting of the Chemical Society on October 15, 1942[3], being at that time particularly interested in the rather remarkable rubber–silver nitrate compound[4], which is another evident example of this structural type.

Similar association between donor and acceptor components has been envisaged by Woodward[5] as the initial step in the Diels–Alder reaction. Pitzer[6] has re-stated the basis of the Winstein – Lucas theory more precisely. Dewar[7] has adduced evidence that donor acceptor complexes condition many rearrangements in aromatic systems, and has emphasized particularly the mobility of the bound quasi-cation over the whole electron cloud of the aromatic nucleus, thus permitting the electrophilic power of the ion to operate at the most favoured carbon centre.

Even quantitative data exist to supplement that provided by ionization potentials as cited by Walsh. Winstein and Lucas measured the heats of complex formation of methylethylethylene and *cyclo*hexene with silver nitrate in aqueous solution, and found them to be nearly half that for the analogous silver ion complex with two molecules of ammonia; and Baughan, Evans and Polanyi[8] have deduced that the proton affinity of ethylene (174 kcal./gm. mol.) is only 10 kcal./gm. mol. less than that of water.

While I now concur with Walsh's preference for a simpler representation of this bonding than a multiple set of canonical structures, this issue is superficial —any symbolism of this kind is, to quote from Ingold, purely intellectual scaffolding.

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[1] Walsh, *Nature*, **159**, 165 (1947). Cf. also *J. Chem. Soc.*, 89 (1947).
[2] Winstein and Lucas, *J. Amer. Chem. Soc.*, **60**, 836 (1938). Cf. Taufen, Murray and Cleveland, *J. Amer. Chem. Soc.*, **63**, 3500 (1941).
[3] A condensed report is given in *Chem. and Ind.*, **61**, 453 (1942).
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[6] Pitzer, *J. Amer. Chem. Soc.*, **67**, 1126 (1945).
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Reduction of Potassium Permanganate in the Presence of Glass

An interesting phenomenon has been recorded during an investigation in which the test for decomposable organic matter, by the determination of the amount of oxygen absorbed by $N/80$ potassium permanganate acidified by 25 per cent (v./v.) sulphuric acid, was employed and of which no previous record can be found.

During the preliminary stages of work on the breakdown of organic matter in lake waters, it was found that a significantly larger amount of oxygen was absorbed from acidified potassium permanganate by *distilled* water in the presence of small glass balls (3–4 mm. diameter) in comparison with the blank in the absence of glass balls. As this effect was likely to interfere seriously with future experiments involving the amount of oxygen absorbed from acidified potassium permanganate by various lake waters, it was necessary to study the effect in some detail; the results have proved to be of considerable interest and are summarized below. The official standard method for oxygen absorbed from potassium permanganate[1] was used throughout, except that in different experiments the period of incubation varied from 4 to 24 hours. Distilled water (100 ml.) from a metal still was used, and in all except the preliminary experiments it was collected in an aluminium container and used at once.

(1) Oxygen is absorbed by distilled water from acid permanganate in the presence of glass balls, crushed plate, bottle and 'Pyrex' glass, and silica (crushed 'Vitreosil'). With similar quantities (100 gm.) of the different types of glass and silica, crushed to approximately the same size-range, and dried and tested under identical conditions, there was no significant difference in the amount of oxygen absorbed by the different materials in view of the possible differences in surface areas involved:

'Pyrex'	Bottle	Plate	Silica
0·74	0·67	0·87	0·63 p.p.m.

(2) With small (3–4 mm.) or larger (10 mm.) glass balls and 'Pyrex' glass, the amount of oxygen absorbed was directly related to the weight of balls used.

Weight of balls	100 gm.	200 gm.	300 gm.
Oxygen absorbed (p.p.m.)	0·50	1·01	1·54
Weight of 'Pyrex' glass	108 gm.	140 gm.	
Oxygen absorbed (p.p.m.)	0·60	0·78	

(3) If, after testing, the glass is washed in the container with distilled water and then tested again, no significant amount of oxygen is absorbed. Drying at 140° C. or at 30° C. reactivates the glass. The material is also reactivated when spread out in an oven at 140° C. in an atmosphere of nitrogen or oxygen. If the material is dried closely packed together, little activation takes place.

Material was treated in following orders:

'Pyrex' glass (108 gm.)	Oxygen absorbed (p.p.m.)	Silica (100 gm.)	Oxygen absorbed (p.p.m.)
Cleaned and dried	0·60	Cleaned, not dried	0·05
Washed and tested again	0·00	Washed, dried in oven, spread out	0·63
Distilled water added, boiled, cooled, and tested	0·09	Dried in atmosphere of O_2, spread out	0·87
Washed and dried in oven, spread out	0·64	Dried in atmosphere of N_2, spread out	1·29
		Washed, not dried	0·06
		Dried, packed in bottle	0·10

(4) Distilled water which has remained in contact with activated glass for 20 minutes or longer is able to reduce potassium permanganate in the absence of the glass. The water from contact with silica or 'Pyrex' was less active than that from bottle or plate glass, but the differences are of doubtful significance in view of the fact that in some cases small fragments of the material remained in the distilled water after decantation.

Type of oven-dried glass in contact (100 gm.)	Distilled water	'Pyrex'	Silica	Plate	Bottle
Oxygen absorbed (p.p.m.)	—	0·24	0·23	0·57	0·77
Relative conductivity (mho × 10^{-6})	2·49	2·54	2·49	3·13	2·90

Control experiments have shown that the initial method of cleaning the glass is not responsible for the reduction of the potassium permanganate, nor is the effect due to adsorption of the liberated iodine on the glass at the titration stage of the test. No explanation of the phenomena observed is offered; it is hoped that some elucidation may be forthcoming from more appropriate quarters. In view of the fact that both silica and 'Pyrex' are effective in reducing permanganate, the effect is not entirely due to the presence of free alkalinity from the material; this point is confirmed by the conductivity measurements. The most striking observation recorded appears to be that glass or silica may be activated whether the atmosphere is of oxygen, nitrogen or free air, but that it is essential for the particles to be well spread out.

Grateful acknowledgment is made to Prof. H. Moore of the Department of Glass Technology, University of Sheffield, for his interest in the problem and for advice in connexion with the chemistry of glass.

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[1] Ministry of Health, "Methods of Chemical Analysis as Applied to Sewage and Sewage Effluents" (London: H.M. Stationery Office, 1929).

Adsorption of Water Vapour in High-Vacuum Apparatus

The measurement of water-vapour pressures in a glass high-vacuum apparatus is susceptible to considerable errors through adsorption, particularly at high water-vapour pressures and low temperatures. This adsorption can be nearly eliminated by the use of a hydrophobic surface, and a simple method of coating the apparatus has been suggested to us by Dr. A. E. Alexander. We find that if the glass surface is treated with a 0·05 per cent solution of 'Cetavlon', $C_{16}H_{33}N^{+}Me_3Br^{-}$, in water, a monolayer is adsorbed giving an external surface equivalent to a hydrocarbon; excess reagent is removed by washing with water. The adsorbed layer is not affected by high vacua, and allows quantitative measurement of pressures of water vapour to be made accurately in accordance with Boyle's law.

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General Equation for the Serial Dilution Technique in Microbiological Assays

The basis of the serial dilution technique is a comparison of a solution of the sample of material under test with a solution of a standard sample of known strength. In order to make the comparison, serial dilutions of both the standard and test solutions must be made; in cases where the potency (or purity) is roughly known to start with, the number of such dilutions necessary is usually four or five. When, however, there is not even a rough indication of the probable potency of the sample being assayed, a wide range of dilutions is involved, some of which will probably be outside the scope of the tables that may be available for the evaluation of potencies in routine work. It seems desirable, therefore, to have at hand a general expression for evaluating the results of a serial dilution procedure; such an expression, apart from its intrinsic interest, will be useful for application in the cases of certain routine samples as well as of investigational work where unpredictable losses of potency may occur.

In deriving the equation, the following serial dilution technique is assumed. A solution of known strength is prepared from the standard sample and diluted to a suitable strength by one or more dilutions. A known weight of the sample under test is dissolved in a known volume of solvent and diluted similarly. Further dilutions of the standard and test solutions are carried out in nutrient broth, the first broth dilution normally (but not necessarily) being the penultimate dilution.

The ultimate dilutions of both standard and test solutions are obtained by adding successively decreasing volumes of the penultimate dilution to a series of tubes each containing the same volume of broth; they consist, therefore, not of one dilution but of a *graded series* of dilutions. (Sometimes a graded series of broth volumes is recommended so that all dilutions have the same volume. Such procedure has the advantage that the results can be written down at sight from the experimental readings, but it is attended by the drawback of an overall loss of time due to the manipulative work involved.) After inoculation and incubation, a member of the graded series of the test dilutions and a member of the graded series of dilutions of the standard which match one another in respect of a particular property are ascertained. These two selected dilutions are regarded as being equal in strength in relation to the substance being assayed, whence the potency of the original sample is calculated.

The general expression for such a serial dilution technique is developed as follows, all weights and volumes being, of course, supposed expressed in consistent units.

An arbitrary potency, P_A, referred to as the 'assumed potency', is assigned to the sample for assay. A weight w of the sample is dissolved in volume V of solvent to form the test solution. The assumed strength of the test solution is then wP_A/V; denote this by u_A, and let the true strength of the test solution be u_T. Suppose volume n_1, of standard solution of strength S, is added to volume N_1 of diluent, thereby forming the first standard dilution, while volume x_1 of test solution is added to volume X_1 of diluent to form the first test dilution. The strengths of the first standard and the first test dilutions will then be $n_1S/(N_1+n_1)$ and $x_1u_T/(X_1+x_1)$, respectively.

To form the second dilutions, suppose volume n_2 of the first standard dilution is added to volume N_2 of diluent, and that volume x_2 of the first test dilution is added to volume X_2 of diluent. Then, the respective strengths of the standard and test solutions in the second dilution stage are

$$\frac{n_2 \cdot n_1S/(N_1+n_1)}{N_2+n_2} \text{ and } \frac{x_2 \cdot x_1u_T/(X_1+x_1)}{X_2+x_2}.$$

If now the rth dilution of the standard is supposed to match the tth dilution of the test solution, where volume n_r of the penultimate standard dilution is added to volume N_r of diluent and volume x_t of penultimate test dilution is added to volume X_t of diluent, then it will be seen that

$$\frac{n_r\, n_{r-1}\, n_{r-2} \ldots n_1S}{(N_1+n_1)(N_2+n_2) \ldots (N_r+n_r)} = \frac{x_t\, x_{t-1}\, x_{t-2} \ldots x_1u_T}{(X_1+x_1)(X_2+x_2) \ldots (X_t+x_t)},$$

whence

$$u_T = S \cdot \frac{[n_r\, n_{r-1}\, n_{r-2} \ldots n_1]\ [(X_1+x_1)(X_2+x_2) \ldots (X_t+x_t)]}{[(N_1+n_1)(N_2+n_2) \ldots (N_r+n_r)]\ [x_t\, x_{t-1} \ldots x_1]},$$

which may be written

$$u_T = S \cdot \frac{\prod_{Z=1}^{r} n_Z \cdot \prod_{Z=1}^{t} (X_Z + x_Z)}{\prod_{Z=1}^{r} (N_Z+n_Z) \prod_{Z=1}^{t} x_Z}.$$

This equation applies where the sample for assay is a solution the strength of which is required. The corresponding equation for the true potency, P_T, is readily obtained therefrom with the aid of the relation $P_T/P_A = u_T/u_A$:

$$P_T = S \cdot \frac{P_A}{u_A} \cdot \frac{\prod_{Z=1}^{r} n_Z \prod_{Z=1}^{t} (X_Z+x_Z)}{\prod_{Z=1}^{r} (N_Z+n_Z) \prod_{Z=1}^{t} x_Z}.$$

The above expressions have found useful application in the examination of samples of penicillin, but they apply generally where a serial dilution technique as outlined above is employed. The adaptation of the equation for u_T to colorimetric analysis is also envisaged.

Thanks are expressed to the Chief Scientist, Ministry of Supply, for permission to publish this note.

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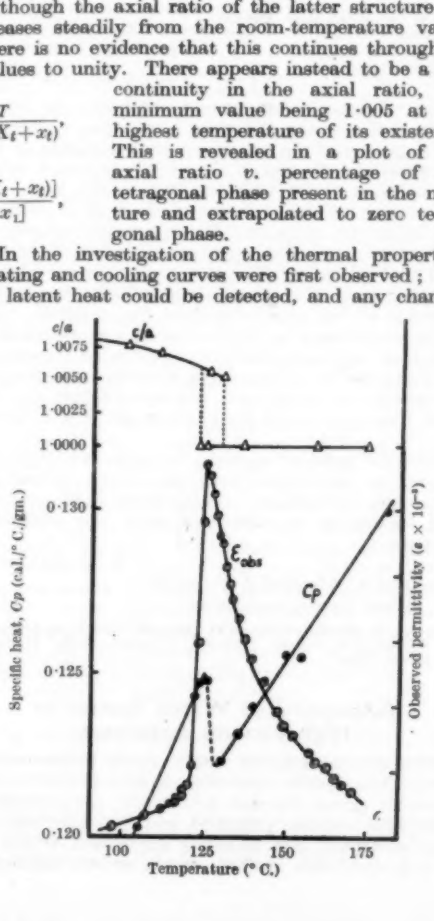
April 16.

Curie Point of Barium Titanate

THE Curie point, that is, the transition temperature between the ferro-electric and the non-ferro-electric structures of barium metatitanate, $BaTiO_3$, is characterized by a marked peak in the permittivity v. temperature curve and has recently received much attention, though reported values[1-4] for the temperatures of maximum permittivity show in some cases considerable discrepancies. This may be due to the effect of impurities or the firing conditions employed. It has also been reported[5] that there is a second-order phase transition from a tetragonal structure to a cubic structure at about 120° C. The identity of the temperature of this transition with that of the permittivity peak has been regarded as uncertain, and we have, therefore, determined the Curie point by two non-electrical methods, namely, X-ray structure determinations and specific heat measurements, and compared these with the permittivity using a material containing more than 99 per cent $BaTiO_3$. That these effects occur at the same temperature has now been established, but a further complexity has been revealed on detailed examination of the tetragonal to cubic transition.

There is a range of temperatures, 122°–129° C., in which the tetragonal and cubic forms co-exist; the cubic phase appears at the lower and the tetragonal disappears at the upper temperature cited above. Although the axial ratio of the latter structure decreases steadily from the room-temperature value, there is no evidence that this continues through all values to unity. There appears instead to be a discontinuity in the axial ratio, the minimum value being 1·005 at the highest temperature of its existence. This is revealed in a plot of the axial ratio v. percentage of the tetragonal phase present in the mixture and extrapolated to zero tetragonal phase.

In the investigation of the thermal properties, heating and cooling curves were first observed; but no latent heat could be detected, and any changes



in the slope at the Curie point were not sufficiently distinct to deduce a discontinuity in the temperature-dependence of the specific heat. As it was obvious that a far more precise technique was required, the specific heat was then determined from point to point by means of a twin calorimeter similar in principle to that used by Rusterholz[4]. The relation thus determined is shown in the accompanying figure. At the Curie point, which occurs at 125° C., there is a change in the specific heat amounting to about 0·0025 cal. per gm. per degree.

The permittivity was determined using a sample prepared by pressing the material into a disk and firing at 1,350° C. A substitution method was used at 1·5 Mc./s., and the results (see figure) show a maximum permittivity at 125° C., corresponding to the middle of the co-existence range for cubic and tetragonal structures. Within this range, the observed permittivity at any temperature is a value between that of the cubic and that of the tetragonal lattice, depending on the ratio between the two phases present. At temperatures above the co-existence range the permittivity (corrected for porosity) follows the Clausius–Mosotti formula fairly accurately with a value of $15{\cdot}3(4) \times 10^{-24}$ c.c. for the polarizability per unit cell, with no dipole contribution, as has been pointed out by van Santen and Jonker[7]. This would theoretically give rise to an infinite permittivity at 118° C., but owing to the change to the tetragonal structure a finite peak is observed. If, however, a bridge circuit fitted with an electronic indicator of balance (for example, a 'magic eye' tuning indicator) is set to a capacity higher than that corresponding to the normal permittivity peak, instantaneous values of permittivity considerably higher than the peak value may be observed when the sample is rapidly heated or cooled through the co-existence range. This we attribute to a finite time of transition between the two phases, resulting in instantaneous permittivities corresponding to those of the separate phases at temperatures at which they would not normally exist or would already be admixed with the other phase.

It is intended to publish fuller details of this work elsewhere. We wish to thank Mr. J. A. M. van Moll and the directors of Philips Lamps, Ltd., for permission to publish this note.

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[2] Coursey and Brand, *Nature*, **157**, 297 (1946).
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Solar Limb Flare and Associated Radio Fade-out, April 15, 1947

In the report of the Astronomer Royal to the Board of Visitors of the Royal Observatory, Greenwich (June 7, 1947), reference is made to the occurrence of a severe magnetic disturbance on April 17–18, and of a major radio fade-out at 14.57 hr. U.T. on April 15, almost 46 hours prior to the commencement of the magnetic storm. No related solar flare had been identified.

Spectrohelioscope observations were made at the Solar Physics Observatory, Cambridge, on April 15 during 15.00–15.15 hr. U.T., until interrupted by cloud. There was nothing of note upon the solar disk; but on the south-west limb two comparatively quiescent prominences were visible with a very bright detached area above. The bright area could be seen in $H\alpha$ (6563 A.) and D_3 (5876 A.); the height above the limb was 2′, and the approximate latitude radially below 50° S. The intensity as a proportion of that of the continuous spectrum of the disk near $H\alpha$ is estimated at 50 per cent (15.00 hr.), 30 per cent (15.05 hr.) and 15 per cent (15.15 hr.). Observations on April 16 showed pronounced prominence activity in the same region, but of more usual brilliance.

It is considered that the radio fade-out is to be associated with this flare, which probably originated in the active areas in or around the great sunspot group of March 31–April 13[1]. This had passed over the limb almost two days previously to the outburst. The abnormal flare position may be responsible for the marked delay in the onset of the magnetic storm. It is noteworthy that no associated geomagnetic 'crochet' or increase in solar radio noise occurred. The previous intense limb flare of February 21, 1942[2], which was also accompanied by a radio fade-out, had a well-pronounced 'crochet'; radio noise observations were, of course, not available.

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June 16.

[1] *Nature*, **159**, 549 (1947).
[2] Stratton, F. J. M., *Nature*, **157**, 48 (1946).

Cross-Sections for Production of Artificial Mesons

Anticipating that mesons may be produced shortly in laboratory experiments by nucleons or photons of a few hundred million volts, we have applied the theory of radiation damping to compute the cross-sections for the production of mesons in two collision processes.

(1) *Nucleon + nucleon → meson + nucleon + nucleon.* For this process, we have used the symmetrical meson theory, in the Møller–Rosenfeld form, with the coupling constant $f_0^2/\hbar c = 0{\cdot}065$. $g_0^2/\hbar c$ has been neglected, and the mass μ of the meson is taken equal to one tenth of the mass of a nucleon. The following results have been obtained.

(*a*) Meson production starts when the kinetic energy E of the incident nucleon is greater than $2\mu c^2$.

(*b*) The total cross-section φ for the production of a meson is given in the following table. (Transverse and pseudo-scalar mesons are produced in the ratio 2 : 1; the values given in the table refer to the sum of transverse and pseudo-scalar mesons.)

Table 1. Meson production by nucleon-nucleon collisions

E (kinetic energy of the incident nucleon)	1·9	2·8	3·8	4·7	$\times 10^8$ eV.
φ for $P+P \rightarrow V+$ (or $N+N \rightarrow V-$)	0	0·80	5·7	16	$\times 10^{-27}$ cm.^{2}
φ for $P+P \rightarrow V^0$ (or $N+N \rightarrow V^0$	0	0·25	1·9	5·2	$\times 10^{-27}$ cm.^{2}
φ for $P+N \rightarrow V+$ and $V-$ (or $N+P \rightarrow V-$ and $V+$)	0	0·27	2·1	5·4	$\times 10^{-27}$ cm.^{2}
φ for $P+N \rightarrow V^0$ (or $N+P \rightarrow V^0$)	0	0·29	2·0	5·9	$\times 10^{-27}$ cm.^{2}

Here, for example, $P + N \rightarrow Y^+$ denotes the production of a positive meson by an incident proton colliding with a neutron which was initially at rest. In a proton-neutron collision, positive and negative mesons are produced almost equally; the values given in the table refer to the sum for both charged mesons.

(*c*) The energy ε of the mesons produced (subtracting the rest energy) varies from zero to $\varepsilon_{max} = \frac{1}{2}E - \mu c^2$, but most of them possess energy $\varepsilon > \varepsilon_{max}/3$.

(*d*) The angular distribution of the mesons produced is uniform.

We have neglected, in the calculation, quantities involving v/c, v denoting the velocity of the nucleons. Actually, for the incident nucleon, $v/c \geqslant 0{\cdot}6$; so all the above results are only approximate. The numerical values for the cross-sections may be correct to within a factor of three or four.

A full account of this work will be published shortly in the *Proceedings of the Royal Irish Academy*. Meson production by nucleon-nucleon collisions in the high energy region ($E \geqslant 2 \times 10^9$ eV.) has already been treated[1] by a different method, where a cross-section of the order of 10^{-28} cm.^{2} has been found. This is consistent with the rapid increase shown in Table 1 in the low-energy region.

(2) *γ-Ray + nucleon $\rightarrow$ meson + nucleon.* The cross-sections for this process have been calculated previously[2], using the charged meson theory with $f^2/\hbar c = 0{\cdot}11$, $g^2/\hbar c = 0{\cdot}17$. Some numerical values have now been calculated for small energies $h\nu$ of the γ-ray, as given in Table 2.

TABLE 2. MESON PRODUCTION BY γ-RAYS

$h\nu$	0·94	1·1	1·3	2·1	3·9	5·7	8·5	$\times 10^8$ eV.
φ longitudinal	0	0·52	1·7	4·1	15	30	46	$\times 10^{-28}$ cm.^{2}
φ pseudoscalar	0	1·8	2·7	3·1	3·7	–	2·3	$\times 10^{-28}$ cm.^{2}

The cross-section for the production of transverse mesons is probably about the same as that of pseudoscalar mesons. These cross-sections, φ_{meson}, for meson production can be compared with those for production of an electron pair, φ_{pair}. For $h\nu \sim 2 \times 10^8$ eV., $\varphi_{pair}/\varphi_{meson}$ is of the order of 200 in lead, or 30 in air (per atom). For $h\nu \sim 5 \times 10^8$ eV. the corresponding ratios are about 70 in lead and 10 in air.

On comparing the two tables, it appears that meson production by γ-rays is comparable with that by nucleon-nucleon collisions in the energy region $2{\cdot}5$–$3{\cdot}5 \times 10^8$ eV.; at lower energies, the production of mesons by γ-rays is more effective, at higher energies that by nucleon-nucleon collisions.

We wish to thank Prof. W. Heitler for suggesting these problems and for many valuable discussions.

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April 17.

[1] Hamilton, Heitler and Peng, *Phys. Rev.*, **64**, 78 (1943). Heitler and Walsh, *Rev. Mod. Phys.*, **17**, 252 (1945).
[2] Hamilton and Peng, *Proc. Roy. Irish Acad.*, **49**, 197 (1944).

Effect of Charge in Turbulent Flow in Alluvium

MR. GERALD LACEY, in his letter published in *Nature* of March 22, reproduced two of his early formulæ in dimensional form

$$P/R = \tfrac{1}{2}(V^2/gR)^{1/3} \cdot (RV/\nu)^{1/3} \qquad (A)$$

$$+V^2/gRS = \tfrac{1}{2}(V^2/gR)^{-2/3}(RV/\nu)^{1/3}. \qquad (B)$$

(Note μ instead of ν was shown in the Reynolds number by oversight.)

In these equations, grade and charge were omitted. Charge can, however, be brought in if formulæ are put in the form recently suggested by Prof. C. M. White, namely,

$$\frac{b.g^{1/5}}{Q^{2/5}} = \alpha_1 \cdot \left(\frac{Q}{m^{5/2}g^{1/2}}\right)^{n_1} \cdot \left(\frac{m(\acute{e}g)^{1/3}}{\nu^{2/3}}\right)^{n_2} \cdot \left(\frac{G}{Q}\right)^{n_3} \qquad (C)$$

and the following procedure is followed:

(i) Vs is substituted for m in $\left(\frac{m(\acute{e}g)^{1/3}}{\nu^{2/3}}\right)$—which is necessary because kinematic viscosity is linked with rate of fall of particles.

(ii) G/Q, or X = the charge is linked with Vs, and

(iii) Lacey's exponents are retained.

A set of formulæ can then be put in the form

$$\frac{b.g^{1/5}}{Q^{2/5}} = \alpha_1 \cdot \left(\frac{Q}{m^{5/2}g^{1/2}}\right)^{n_1} \cdot \left(\frac{XVs}{(\nu g)^{1/3}}\right)^{n_2}. \qquad (D)$$

The linking of X with Vs is justified on two grounds:

(*a*) An investigation carried out at Poona under my direction had shown that the rate of deposition of material in water was constant so long as the product $(X.Vs)$ remained constant[3]; that is, so long as X varied inversely as Vs. This was the case where the material was quartz sand and m was greater than about 0·15 mm. and less than about 0·5 mm.; but for grains smaller than 0·08 mm., Stokes' law held and $Vs \propto m^2$; and for grains coarser than about 0·7 mm., $Vs \propto m^{1/2}$.

(*b*) Experiments initiated by me at Poona, when I was director of the Indian Waterways Experiment Station, had shown that when the 'grade' of material was kept constant and the 'charge' varied, the exponents were similar to those in the new set of formulæ, when the exponents were based on the Lacey exponents.

The full set of derived formulæ are:

New formulæ	Lacey equivalents
$b = \alpha_1 \cdot \frac{Q^{1/2}}{g^{1/2}\nu^{1/12}} \cdot \left(\frac{XVs}{m}\right)^{1/4}$	(1) $P = 2{\cdot}67\,Q^{1/2}$
$A = \alpha_2 \cdot \frac{\nu^{1/36}}{g^{7/12}} \frac{Q^{5/6}}{(m\,.\,XVs)^{1/12}}$	(2) $A = \frac{1{\cdot}26\,Q^{5/6}}{f^{1/2}}$
$V = \alpha_3 \cdot \frac{g^{7/12}}{\nu^{1/36}} Q^{1/6}\,(m\,.\,XVs)^{1/12}$	(3) $V = 0{\cdot}7937\,Q^{1/6}\,.\,f^{1/2}$
$d = \alpha_4 \cdot \frac{\nu^{1/9}}{g^{1/18}} \cdot \frac{Q^{1/3}m^{1/6}}{(XVs)^{1/3}}$	(4) $R = 0{\cdot}4725\left(\frac{Q}{f}\right)^{1/3}$
$S = \alpha_5 \cdot \frac{(m\,.\,XVs)^{5/12}}{\nu^{5/36}g^{1/18}Q^{1/6}}$	(5) $S = 0{\cdot}000547\,\frac{f^{5/3}}{Q^{1/6}}$
$(S.V) = \alpha_6 \cdot \frac{g^{1/2}}{\nu^{1/6}}(m\,.\,XVs)^{1/2}$	(6) $(S.V) = 0{\cdot}000434\,f^2$
$\frac{b}{d} = \alpha_7 \cdot \frac{Q^{1/6}(XVs)^{7/12}}{g^{5/18}\,.\,\nu^{7/36}m^{5/12}}$	(7) $\frac{P}{R} = 5{\cdot}65\,Q^{1/6}\,.\,f^{1/2}$
$M_1 = \alpha_8 \cdot \frac{Q^{1/2}}{g^{1/2}\nu^{1/12}} \cdot \left(\frac{XVs}{m}\right)^{1/4}$	(8) —

[3] Lacey, *Proc. Inst. Civ. Eng.*, **229**, 259 (1930).

$$\frac{V^2}{gd} = \alpha_9 \cdot \frac{(XVs)^{1/3}}{(g\nu)^{1/6}} \quad \text{(Froude No.)} \qquad (9)\ \frac{V^2}{R} = \frac{4}{3} f$$

$$\frac{Vd}{\nu} = \alpha_{10} \cdot Q^{1/3} \cdot \frac{g^{1/3}}{\nu^{11/12}} \cdot \left(\frac{m}{XVs}\right)^{1/4} \quad \text{(Reynolds No.)} \qquad (10)\ \frac{VR}{\nu} = 0{\cdot}375\ Q^{1/3}$$

Where b = breadth; A = area; V = velocity; d = mean depth; b/d = shape factor; S = slope; M_l = meander length; $(S.V)^{1/3}$ = Lacey's new silt factor; R = hydraulic mean depth; P = wetted perimeter; $f = 0{\cdot}75\ V^2/R$ = Lacey's original silt factor, and (SV) = Lacey's new sand factor.

By reducing Mr. Lacey's (A) and (B) formulæ, we obtain

$$P/R = \tfrac{1}{2}\ (V^2/gR)^{1/3} \cdot (RV/\nu)^{1/3}, \qquad (A)$$

which reduces to

$$P = \tfrac{1}{2} \frac{VR}{(g\nu)^{1/3}} \qquad (A1)$$

$$\text{or } P = \sqrt{\frac{Q}{2(g\nu)^{1/3}}} = 2{\cdot}78\ Q^{1/3} \text{ (at 30° C.)}, \qquad (A2)$$

$$\text{and } V^2/gRS = \tfrac{1}{2}\ (V^2/gR)^{-2/3} \cdot (RV/\nu)^{1/3} \qquad (B)$$

$$\text{or } V = g^{5/6}/\nu^{1/6} \cdot R^{2/3} S^{1/3} \qquad (B1)$$

$$= 15{\cdot}8\ R^{2/3}\ S^{1/3} \text{ (at 30° C.)}. \qquad (B2)$$

$(B2)$ is what Lacey has called his "general regime formula"[2].

Though dimensionally homogeneous, these two formulæ omit the effect of charge and grade, whereas grade and charge are included in formulæ (1) and (3).

When $R^{2/3}$ and $S^{1/3}$ in Lacey's (B) formula are rewritten in terms of the new equations we obtain

$$V \propto \frac{\nu^{1/24}}{g^{1/12}} \cdot Q^{1/6} \cdot \frac{m^{1/6}}{(XVs)^{1/12}}. \qquad (3a)$$

This differs from equation (3), which is not directly deducible from $(B1)$ because, as I pointed out in 1936 [4], this formula should be in the form

$$V = 16{\cdot}0\ R^{2/3}\ S^{1/3}\ (f_{Vd}/f_{dS})^{1/3}, \qquad (9)$$

where the silt factors $f_{Vd} = 0{\cdot}75\ V^2/d$ and $f_{dS} = 192\ d^{1/3}\ S^{2/3}$.

Equation $(3a)$ should, therefore, be rewritten in the form

$$V \propto \frac{\nu^{1/24}}{g^{1/12}} \cdot Q^{1/6} \cdot \frac{m^{1/6}}{(XVs)^{1/12}} \cdot \frac{g^{1/6}}{\nu^{1/12}} \cdot \left(\frac{XVs}{m}\right)^{1/6}$$

or $V \propto g^{7/12}/\nu^{1/24} \cdot Q^{1/6}\ (m \cdot XVs)^{1/12}$, which is identical with equation (3).

Thus grade and charge should not be omitted in this equation, though they come in to such a low power that they have a negligible effect in the sand region, where $Vs \propto m$, and not much effect even in the regions where $Vs \propto m^{1/3}$, or m^2.

The above formulæ are for quartz sand in water; if any other material or liquid is used, $m(\sigma - \rho)/\rho$ is involved, where σ is specific gravity of material and ρ of liquid.

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May 9.

[1] Central Irrigation and Hydrodynamic Research Station, Poona. Annual Reports (Technical), 1940–41, p. 50; 1941–42, p. 33.
[2] "The Behaviour and Control of Rivers and Canals (with the aid of Models)", chapter 3, by the Author (in the press).
[3] Paper 5518, Inst. Civ. Eng., "A General Theory of Flow in Alluvium", p. 20.
[4] Discussion on Dr. N. K. Bose's Punjab Engineering Congress Paper 192, "Silt Movement and Design of Channels".

Turbulent Flow in Alluvium

MY communication dated December 9, 1946, published in the issue of *Nature* of March 22, 1947, pp. 407–8, contains an error, due to hasty transcription, for which I owe an apology to those who have attempted to follow the derivation of the dimensionless equations. The seventh essential variable, the energy gradient i, should have been given as ρgS, and not as gRS. The kinematic viscosity ν has also on p. 408 been replaced by μ the viscosity. The Reynolds number should appear as (RV/ν) throughout.

The correct equations were quoted by me[1] in 1937 in the more general form

$$iR/\rho V^2 = gRS/V^2 \propto (RV/\nu)^{-1/3}\ (V^2/gR)^{2/3},$$

and

$$P/R \propto (RV/\nu)^{1/3}\ (V^2/gR)^{1/3}.$$

No attempt was made at that time to assign numerical values to the constants, or to eliminate the Reynolds number, a step which in retrospect appears sufficiently obvious.

I should have stated finally in respect of the equations that they can apply rigidly only to an ideal self-generating channel flowing in an unlimited medium of incoherent alluvium identical with the alluvium transported.

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[1] *Trans. Amer. Soc. Civ. Eng.*, **102**, 159 (1937).

Role of Dendritic Cells in the Infective Colour Transformation of Guinea Pig's Skin

WHITE skin from a spotted black and white guinea pig may be caused to turn black by grafting it to a pigmented area. Conversely, black skin grafted to a white area slowly blackens the white skin that surrounds it[1,2]. Recent experiments by Billingham and Medawar[2] have set aside the possibility that the blackening reaction is the outcome of a mere diffusive process, or of a mass replacement of white epidermal epithelium by black. We have now examined the possibility, for various reasons unfairly belittled in our earlier communication, that the blackening reaction is due to the differential migration of melanoblasts from pigmented into unpigmented skin.

Examined in living black epidermis, melanoblasts (pigmentary dendritic cells) appear clearly as nucleated cells occupying the lower reaches of the epidermis and sometimes just abutting into the underlying dermis. Dendrites originating from them —most commonly four to six primary stalks with distal dichotomizing branches often 100 μ in length —weave horizontally and upwards between the ordinary basal layer cells, which they supply with melanin granules in a manner to be described in detail elsewhere[3]. Black dendritic cells are strongly 'Dopa'-positive, that is, they cause the rapid intracellular oxidation of 3 : 4 dioxyphenylalanine[4], a

likely precursor of melanin[5], in weakly alkaline solution. Even where most densely distributed, the majority of dendritic cells are separate from one another; but we have observed (*a*) confluence of dendrites, and (*b*) the formation of end-caps from the processes of one dendritic cell on the cell body of another—caps similar to those which the dendrites normally make upon the ordinary basal layer cells to which they supply pigment.

Cells similar in structure, number, position, and cellular interrelationships have now been found in the *white* skin of spotted guinea pigs. These white dendritic cells are totally 'Dopa'-negative and neither form nor contain melanin granules. They are invisible in ordinary histological preparations and in living epidermis, and have so far been shown up only by metallic impregnation.

When white skin is grafted to a black area, or *vice versa*, unpigmented dendritic cells are in effect placed next door to black. Since dendritic cells can establish very intimate cytoplasmic connexions with each other and with ordinary basal layer cells, there is a *prima facie* case for supposing that pigmentary dendritic cells can transform their newly acquired white neighbours into cells forming pigment. White dendritic cells so transformed can propagate the transforming agent to others in their turn[2], as well as introducing formed melanin granules into the ordinary basal layer cells of their intermediate domain. This interpretation supersedes our earlier suggestion that the 'infective' process is mediated by ordinary epidermal cells, though we do not yet exclude the possibility that infection may be spread by the common termination of dendrites from white and black dendritic cells on the same epidermal cell, or the possibility that an ordinary epidermal cell, once infected, can propagate the colour transformation to its own lineal descendants.

The infection hypothesis at once explains two crucial experimental facts. An unpigmented epidermal epithelium lacking white dendritic cells should resist infection. We have been unable to detect dendritic cells in the epidermal epithelium of the guinea pig's tongue, and even the smallest tongue grafts transplanted to areas of black skin remain white indefinitely. Moreover, dendritic cells are concentrated in the hair bulbs and in the basal layers of the superficial epidermis; in the outer root-sheath of the hairs they are sparse or absent, and they are absent from that part of the neck of the mature follicle into which the sebaceous glands open. This accounts for the fact that infection normally spreads across the superficial epidermis but not down the follicles[1,2]; for the follicle necks, lacking a contiguous system of dendritic cells, cannot mediate the passage of the infective agent. The infection theory also accounts for the quantitative properties of the blackening process, for example, the uniformly reticulate pattern of spread in white skin, no denser proximally than at its farther boundary; and the fact that the rate and pattern of blackening of white dorsal skin, ear skin and sole of foot grafts correspond exactly with the density and distribution pattern of dendritic cells within them. The alternative theory, of melanoblast migration, accounts for none of these facts and is inconsistent with some of them; but what is even more damaging to it is the present discovery that white dendritic cells are already present in the very positions into which (*ex hypothesi*) the melanoblasts are supposed to migrate. We have not, in any case, found that melanoblasts can migrate away from adult skin epithelium, even when offered favourable conditions for doing so.

The infective transformation of one cell by another must be a very rare phenomenon in higher animals. The case we have studied is particularly favourable because it concerns a cell which establishes very intimate cytoplasmic connexions with its neighbours, and which exists in two or more obviously distinct and true-breeding forms in one and the same individual. It may be added that the infective transformation we have described takes place very slowly at the colour transition zones of spotted guinea pigs during their normal growth. Grafting operations speed up the process and bring it under experimental control.

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May 20.

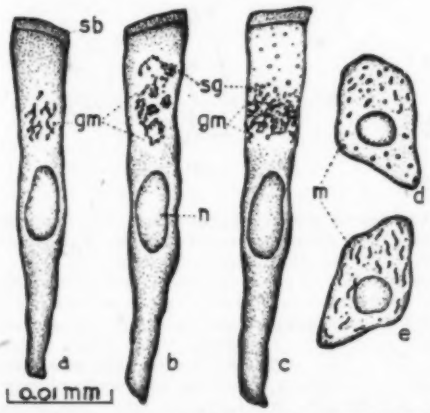
[1] Carnot, P., and Defiandre, C., *C.R. Soc. Biol. Paris*, **48**, 178, 430 (1896); Loeb, L., *Arch. EntwMech. Org.*, **6**, 1 (1897); Saxton, J. A., Schmeckebier, M. M., and Kelley, R. W., *Biol. Bull.*, 71, 453 (1936); Fessler, A., *Brit. J. Dermatol.*, **53**, 201 (1941); Lewin, M. L., and Peck, S. M., *J. Invest. Dermatol.*, **4**, 483 (1941).
[2] Billingham, R. E., and Medawar, P. B., *Nature*, **159**, 115 (1947).
[3] Billingham, R. E., unpublished observations.
[4] Bloch, B., *Amer. J. Med. Sci.*, **177**, 609 (1929).
[5] Raper, H. S., *Biochem. J.*, **21**, 89 (1927).

Cytology of Alimentary Tract and Associated Glands of the Fowl, *Gallus domesticus*

The changes in the cytoplasmic components of the cells of the alimentary tract during fasting and after feeding have been described for several animals of widely separated groups, but, so far as I am aware, there are only three papers on the cytology of the digestive glands of the domestic fowl[1,2,3], and knowledge is still scanty regarding the behaviour of the cytoplasmic inclusions of these structures. The present observations were carried out on fixed material obtained from young chickens, and yielded information which does not seem to have been previously recorded. Samples from different parts of the intestinal tract and from the associated glands were taken from birds killed after a twenty-four hours fast and at periods ranging from half an hour to six hours after a meal.

It was found that a twenty-four hours fast brings about a phase of complete inactivity in practically all the gland cells investigated, and that contact with food causes the cells to become active again. The Golgi material and mitochondria undergo changes of structure and disposition which are closely correlated with the phases of cell activity. The nature of the morphological changes, their intensity and rate of change, vary greatly and are characteristic of each particular group of cells. The mucus-secreting cells, both of the salivary glands and of the intestinal goblet cells, appear to be more autonomous in their action and less capable of being influenced directly by the intake of food than the other cells studied. Besides variations in the rhythm of activity between the cells of different glands, there are differences between particular cells of the same gland. Some gland cells, such as the gastric and pancreatic cells, do not appear to become wholly inactive after a short fast, but exhibit a more or less constant secretory balance depending on the intake of food and

periods of fasting. Their reaction to feeding is much less pronounced than that of the other non-mucous gland cells. The cells of the intestinal epithelium are easily brought to the resting stage by short periods of fasting, and become strongly sensitized to the subsequent administration of food; their cytoplasmic inclusions show profound morphological changes immediately upon direct contact with food (*a*, *b*, *c* in illustration). Marked changes in the Golgi material in the upper part and their gradual decline and total disappearance in the posterior part of the small intestine are no doubt connected with the functions of the different parts of the intestinal lining.



a, *b*, *c*. CELLS OF THE DUODENUM OF THE FOWL, SHOWING GOLGI MATERIAL: (*a*) AFTER 24 HOURS FAST; (*b*) AFTER FEEDING, UPON DIRECT CONTACT WITH FOOD; (*c*) ONE HOUR AFTER FEEDING. *d*, *e*. CELLS OF THE LIVER OF FOWL, SHOWING MITOCHONDRIA: (*d*) AFTER 24 HOURS FAST; (*e*) TWO HOURS AFTER FEEDING *gm*., Golgi material: *m*., mitochondria; *n*., nucleus; *sg*., secretory granules; *sb*., striated border

Although the final product of activity varies in different types of cell, certain constant morphological changes always accompany its production. The Golgi material always shows marked changes under different physiological conditions, and the final elaboration of secretory granules always takes place in the Golgi field. Hypertrophy of the Golgi material and its increased power to reduce osmium tetroxide during cellular activity in the upper part of the alimentary tract shows that the Golgi material actively participates in secretory phenomena, and that it is not a structure with permanent form, but is a specific substance which appears in different forms depending on the functional stage of the cell. The changes in the mitochondria do not suggest their direct participation in secretion. They are least marked in the pancreas and most striking in the liver cells, and are concerned almost exclusively with their orientation in the cell (*d*, *e* in illustration). It is highly probable that the changes undergone by these cell components are more a reflexion of cell activity, as Pollister[4] assumes, than of their direct participation in the secretory process.

It is hoped to publish a more detailed account of this work.

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[1] Argesanu, S., and May, R. M., *Arch. Anat. Micr.*, **34** (1938).
[2] Dalton, A. J., *Anat. Rec.*, **58** (1933).
[3] Hibbard, A., *J. Morph.*, **70** (1942).
[4] Pollister, A. W., *Phys. Z.*, **14** (1941).

Hæmagglutinins of the *Hæmophilus* Group

WE have observed that the erythrocytes of man, mouse, fowl and other animals are agglutinated by saline suspensions of *Hæmophilus pertussis*, *parapertussis* and *bronchisepticus*, and also by filtrates and supernates of casein digest broth cultures of these organisms. The effect is neutralized by human and animal immune sera. A characteristic rise and fall in anti-hæmagglutinin titre occurs in the sera of children during the course of whooping cough. The protective power of sera, given parenterally, against lethal intranasal doses of *H. pertussis* in mice is closely correlated with their anti-hæmagglutinin titres, but not with their content of bacterial agglutinin or antitoxin.

Freshly isolated strains of *H. pertussis* are rich in hæmagglutinin; but the content falls, more or less rapidly, on repeated subculture, even though there is no change in phase, as judged by bacterial agglutination. There is a close correlation between the hæmagglutinin content of strains, their virulence for mice by the intranasal route, and the antigenic potency of vaccines prepared from them in experimental murine pertussis. Virulent hæmolytic strains of *H. bronchisepticus* are rich in hæmagglutinin, which is not present in the avirulent, non-hæmolytic variants.

Bacteria-free filtrates or supernates of broth cultures of *H. pertussis*, with adequate hæmagglutinin content, immunize mice against intranasal infection as efficiently as do vaccines prepared from the washed and re-suspended organisms, or from cultures on Bordet–Gengou medium. The hæmagglutinin in such filtrates, however, is labile and is not converted into toxoid by formalin.

Details of the experiments on which the foregoing statements are based will shortly be published; the fact that field trials of various whooping cough vaccines are at present in progress has prompted this note.

Saline extracts of smooth strains of *Hæmophilus influenzæ* contain a substance which is adsorbed to erythrocytes. This substance does not cause the red cells to agglutinate, but cells treated with it are specifically agglutinated by therapeutic sera prepared by immunization of rabbits with smooth strains of *H. influenzæ*. The substance is not the toxin described by Dubos[1], since it is obtainable only from smooth strains, whereas Dubos found[2] (we have confirmed his finding) that the toxin can be extracted from the rough variants also. Red cells exposed to solutions of the type-specific polysaccharide of Type *B* are not agglutinated by Type *B* immune sera, but absorption of Type *B* sera with the polysaccharide removes their power of agglutinating erythrocytes treated with saline extracts. The fraction in saline extracts of *H. influenzæ* which is adsorbed to erythrocytes appears to be, therefore, a combination of the specific polysaccharide with some other substance.

Erythrocytes which have been exposed to this fraction of *H. influenzæ* are no longer agglutinable by suspensions of influenzal virus in the Hirst test, or by the hæmagglutinin of *H. pertussis*.

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[1] Dubos, R. J., *J. Bact.*, **43**, 77 (1942).
[2] Dubos, R. J., personal communication (1947).

NATURE OF THE C/D-RING UNION IN THE ŒSTROGENIC HORMONES

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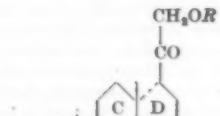
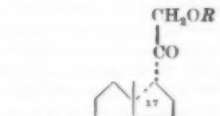
THERE are certain types of biological activity (carcinogenic, œstrogenic, androgenic, progestational and cortical) in which, although little or nothing is known of the mechanism of action, the chemical structures of the primary agents are rather precisely known. While potent carcinogenic and œstrogenic activity is characterized by very low specificity to molecular type, and high androgenic, progestational, and cortical activity is associated in each case with a single specific molecular type, all five types of activity are sensitive to stereochemical structural modification. Thus deoxycorticosterone acetate (I) possesses high cortical activity, whereas 17-*iso*deoxycorticosterone acetate (II), which differs only in configuration at C_{17}, is completely inactive[1]; similarly the activity of progesterone (III) disappears entirely in the epimeric 17-*iso*progesterone (IV)[2].



(I)



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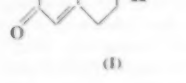

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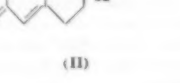
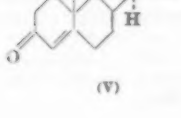


(IV)

The same point is illustrated for androgens by testosterone (V) and *cis*-testosterone (VI), the activity of which is only about $\frac{1}{25}$ of the former[3], and for œstrogens by œstradiol-3 : 17(α) (VII) and œstradiol-3 : 17(β) (VIII), the activities of which[4] are in the ratio of about 1 : 1/40, and by hexœstrol (IX), *d*- and *l*-*iso*hexœstrol (X), the activities of which[5] are roughly as 1 : 1/100 : 1/1,000.



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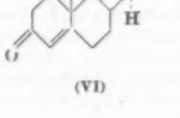

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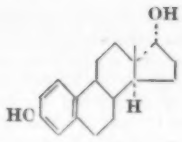

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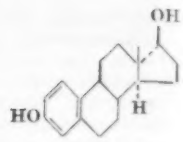

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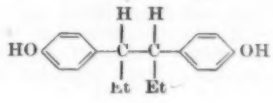

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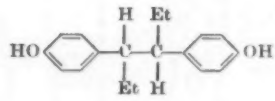
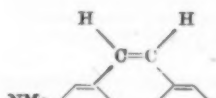
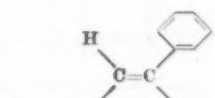


(X)

While most carcinogens are essentially two-dimensional, flat, plate-like molecules, so that stereoisomerism of the foregoing type does not arise, and hydrogenation to three-dimensional molecules invariably leads to loss of carcinogenic activity, stereochemical arrangement can also be an important factor in relation to activity in this group; thus, of the *cis*- (XI) and *trans*-4-dimethylaminostilbenes (XII), the latter, in which the rings are coplanar, but not the former, in which the rings are mutually inclined, exhibits biological activity[6].

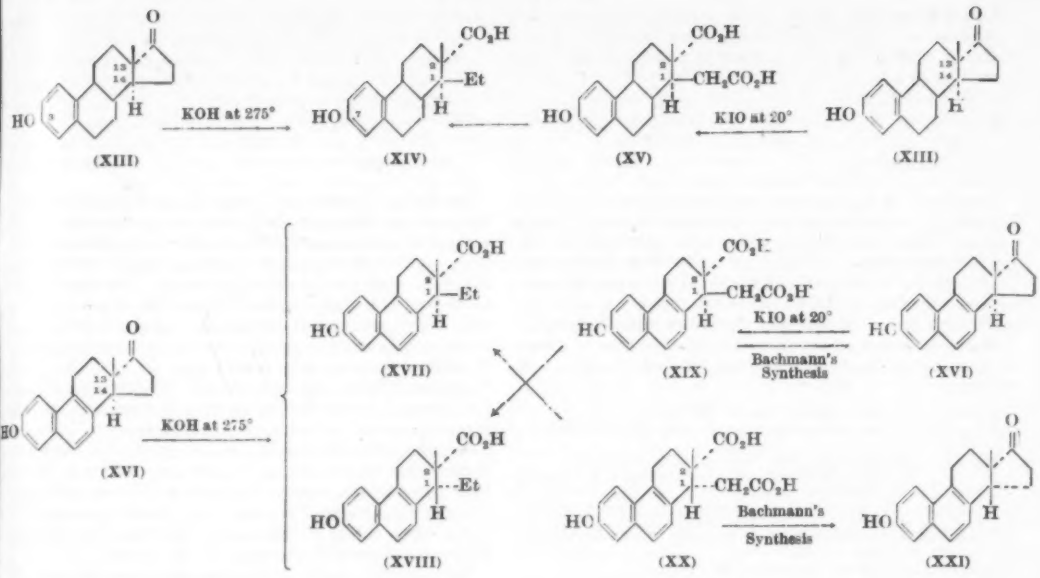


(XI)



(XII)

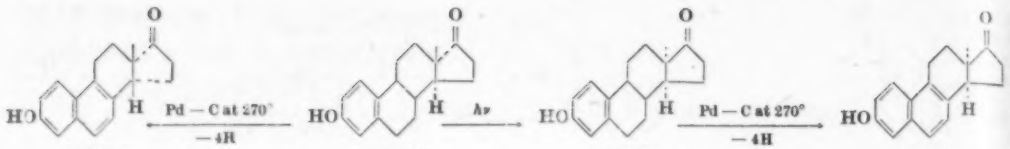
The view that minor molecular modifications, even stereochemical, may cause almost complete loss of physiological activity appeared to be supported by the recent work of Miescher *et al.*[7] on œstrogenic carboxylic acids. (+)Œstrone (XIII) or its dihydro-derivative œstradiol by fusion with potassium hydroxide at 275° gives (+)doisynolic acid (XIV), which is as potent œstrogenically as (+)œstrone (threshold dose by single subcutaneous administration in rats, 0·7γ); (+)equilenin (XVI) or its dihydro-derivative by similar treatment both yield a mixture of two diastereoisomeric acids, (−)'α'(*n*)bisdehydrodoisynolic acid (XVII), which is intensely œstrogenic (dose 0·05γ), and (+)'β'(*iso*)bisdehydrodoisynolic acid (XVIII), which is relatively practically non-œstrogenic (dose 100γ), so that the configurational difference between (XVII) and (XVIII) leads to a 2,000-fold change in activity. The racemic 'α'- and racemic 'β'-bisdehydrodoisynolic acids have been prepared by total synthesis, and the biologically potent racemic 'α'-acid (dose 0·1γ) resolved to give the 'natural' (−)'α'-acid (dose 0·05γ) and the enantiomorphous (+)'α'-acid (dose 10γ), so that the stereochemical difference between the enantiomorphs involves a 200-fold change in activity.



More recently Heer and Miescher[8] have correlated the configurations at C_1 and C_2 of the doisynolic acids (XIV), (XVII), (XVIII) with those of the marrianolic acids (XV), (XIX), (XX), with surprising and disturbing results. By contrast with the extremely drastic conditions of preparation of the doisynolic acids, the marrianolic acids are obtained from œstrone (XIII) and equilinin (XVI) under very mild conditions by an oxidative fission which should not disturb the stereochemical arrangement, so that configuration at C_1 and C_2 in (XV) and (XIX) should correspond with configuration at C_{14} and C_{13} in (XIII) and (XVI); and this is so, for the 'natural' (+)'β'bisdehydromarrianolic acid (XIX) obtained from (+)equilenin (XVI) has been shown to be the (+)-enantiomorph of the synthetic racemic 'β'-bisdehydromarrianolic acid from which Bachmann[9] synthesized racemic equilenin. Now by a series of reactions (Rosenmund reduction of the acid chloride and modified Wolff–Kishner reduction of the resulting aldehyde) which should not involve configurational change at C_1 or C_2, 'natural' (+)marrianolic acid (XV) has been converted into 'natural' (+)doisynolic acid (XIV) in accord with expectation, but 'natural' (+)'β'bisdehydromarrianolic acid (XIX) yields the almost non-œstrogenic (+)'β'bisdehydrodoisynolic acid (XVIII), whereas the racemic 'α'-bisdehydromarrianolic acid (XX), from which Bachmann[9] synthesized racemic *iso*equilenin (XXI), gives the intensely œstrogenic racemic 'α'-bisdehydrodoisynolic acid (XVII).

Retention of the existing formulæ for the doisynolic acids (XIV), (XVII), (XVIII), whereby the biologically potent acids (XIV), (XVII) have the same configuration at C_1 and C_2, requires (*a*) inversion of configuration at C_1 in the second (XIX → XVIII) and third (XX → XVII) transformations but not in the first (XV → XIV), or (*b*) that the formulæ (XVI, XXI) previously attributed to equilenin and *iso*equilenin must be interchanged, that is, that the union of rings C and D in the natural œstrogenic hormones œstrone and equilenin must be different. Both these alternatives conflict with the evidence, summarized above, regarding the relation of stereochemical arrangement to physiological activity.

Finally, it may be pointed out that, while there is a mass of convincing chemical evidence that in the natural androgenic hormones (androsterone, dehydro*iso*androsterone, testosterone (V)), progesterone (III), and the natural adrenocortical hormones (deoxycorticosterone (I), corticosterone, 11-dehydrocorticosterone, Reichstein's substances *S*, *M*, and *F*) rings C and D are united by *trans*-fusion as in the sterols[10] and bile-acids[11], the stereochemical correspondence of œstrone (XIII) to equilenin (XVI) in respect of the mode of linking of rings C and D is not beyond all doubt. The syntheses from cholesterol of œstrone[12] and of 'α'-œstradiol[13] (XII) (recently confirmed[14]) involve pyrolyses at 500–600° and 380° respectively, conditions under which inversion of configuration at C_{14} cannot be excluded. The reported total synthesis of racemic œstrone[15] by a Diels–Alder reaction involving citraconic anhydride, if substantiated, suggests indeed that the mode of linkage of rings C and D must be *cis*-fusion. The conversions of dehydroneoergosterol to œstrone[16], of equilenin to œstrone[17], and of 'α'- and 'β'-dihydroequilenin to 'α'- and 'β'-œstradiol respectively[17] claimed by Marker should be decisive, but have failed to receive independent confirmation during the last nine years; until the promised experimental details are published, the work cannot be evaluated. The experiments of Butenandt[18,19] are also inconclusive; (+)œstrone (XIII), by irradiation with monochromatic ultra-violet light ($\lambda = 313$ mμ), undergoes an irreversible one-quantum process with inversion at C_{13} only to give the physiologically inactive (−)lumiœstrone (XXII), which by dehydrogenation gives (−)*iso*equilenin (XXI*b*), while the parallel dehydrogenation of (+)œstrone gives, not (+)equilenin (XVI), but (+)*iso*equilenin (XXI*a*).



(XXIa) (XIII) (XXII) (XXIb)

Inversion at C_{14} must occur in *one* of these dehydrogenations, even if the biologically inactive *iso*equilenin (dose >500γ) has not, as previously thought, a *cis*-C/D-ring junction (XXI*a*, XXI*b*), but the *trans*-C/D-ring union hitherto attributed to the biologically active equilenin (XVI; dose, *c.* 30γ) by analogy with œstrone. Whatever the stereochemical relationship between œstrone and equilenin, one or other of the conflicting alternatives, stated above, will remain.

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GLACIOLOGICAL RESEARCH

By GERALD SELIGMAN

A NUMBER of scientific expeditions to polar regions are under consideration and in preparation at the present time. In no part of the globe are there more glaciological problems awaiting solution than in the Antarctic. In recent years many important new discoveries in glacier physics have been made, especially north of the equator, and they naturally urge us to find parallels in the Antarctic where less research has been done than elsewhere.

The important climatological work of Prof. H. W. Ahlmann, who has made careful measurements of the economy of northern glaciers, calls for similar work in the south. The results in the north indicate a general recession of the ice, and the question arises whether this is also the case in the great Antarctic glaciers. This is of considerable importance, not only in the long-term effects but also in the present, for the weather of the southernmost inhabited countries is closely linked up with Antarctic snow conditions. Any changes, therefore, in polar regions will be fairly certain to be echoed in these countries.

Recently, the Royal Geographical Society and the Scott Polar Research Institute of Cambridge formed a joint research committee, under the chairmanship of Lord Wakehurst, to co-ordinate polar research on scientific and geographical subjects. The committee requested the British Glaciological Society to formulate a programme of promising fields for snow and ice research with special reference to the Antarctic. A similar request had been made in 1939 by Prof. F. Alton Wade, senior scientist of Admiral Byrd's projected United States Service Expedition to the Antarctic. As a result, a symposium was held on July 12, 1939, at the Royal Geographical Society's house, and the report of it was sent to Prof. Wade. This programme formed the basis of the expedition's glaciological researches and would have been carried out almost in its entirety but for the War cutting short the Expedition's stay in the south.

The success of the 1939 discussion encouraged the Society to adopt this method again, and a meeting took place at the Department of Geography, Cambridge, on May 14, 1947. A number of experts in kindred subjects attended. These included Prof. C. A. Hart, Department of Photogrammetry, University of London; Mr. L. G. Dobbie, Australian Scientific Research Liaison; Dr. C. E. P. Brooks, Meteorological Office, Air Ministry; and Dr. J. N. Carruthers, oceanographer to the Hydrographer of the Navy. The Rev. W. L. S. Fleming, director of the Scott Polar Research Institute, presided.

A list of subjects had been prepared before the meeting in order to direct discussion into channels. This was, in effect, an amplification of the programme prepared for Prof. Wade in 1939 but brought up to date in the light of recent knowledge. It was, however, conceived on a broader basis; there is practically no glaciological problem which can be said to be peculiar to any given area of the world. Conditions may vary in glaciers in Greenland, the Himalayas, the Alps and Graham Land, but the differences are those of degree only. Shelf ice may be considered typical of the Antarctic; nevertheless, evidence of similar formations in the Arctic are believed not to be entirely absent. Therefore, the programme can, broadly speaking, be considered to be very nearly complete for snow and ice research in all parts of the world. The only conspicuous omission is that of the study of the permanently frozen ground covering vast areas of Siberia and Canada, which involves interesting questions of meteorology, recent geology and ice physics.

Scientific workers about to go on expeditions frequently ask for profitable lines of snow and ice research. In my opinion the newly evolved programme should supply material for investigation for some years to come. Selections from it could be made which are in accord with the investigators' interests and resources. A verbatim report of the discussion will be published, from which he will be able to ascertain with whom he must place himself in touch in order to obtain detailed information. Such information cannot form part of a short article

and, indeed, it is not easy to elaborate the bare list of subjects without transgressing the limits set. But mention must be made of one point that emerged during the symposium, namely, the great promise that is held for the advancement of glacier physics. This has been perhaps the chief interest of the British glaciologists since Forbes and Tyndall, and later Deeley and Tutton, carried out their quests in the Alps. There has now been formed a Glacier Physics Committee on the initiative of Dr. M. F. Perutz of the Cavendish Laboratory and under the chairmanship of the Society's President. Several distinguished men of science have joined it in order to give assistance in subjects not normally part of glaciology but which will profoundly affect the course of the contemplated research.

The Glacier Physics Committee is in contact with Swiss glaciologists, and this combination should be able to make important advances in their main theme —the mechanism of glacier flow. This has been a source of controversy for nearly two and a half centuries and, although the subject of much research and a good deal more speculation, there has never been a really well organised, systematic attack on the problem. It is not only of pure glaciological interest; it has been pointed out that a flowing glacier may be likened to a greatly accelerated rock mass in process of translation and recrystallization, and there are other obvious analogies, especially in metallurgy, to the behaviour of ice under stress.

It is only possible to single out two other points upon which discussion centred, namely, the climatological factors touched on above and the movement of the pack ice, so important for whaling and for shipping generally.

The wide field covered by the word 'glaciology' has had many brilliant exponents in Great Britain, but it cannot be said that there has been a regular school of research as there has been in other countries. It was not until after the meeting of the International Union of Geodesy and Geophysics in Edinburgh in 1936 that an atmosphere of continuity began. Since then, except for the war years, interest has increased steadily, and the science now seems to be on a firm basis and the course set for intensive work.

The full report of the meeting will be published in the Society's *Journal of Glaciology*. A detailed exposition of the programme proposed for the Glacier Physics Committee will be found in the *Journal of Glaciology*, Vol. 1, No. 2, pp. 45–51.

RECENT RESEARCH ON LOCUSTS

THE establishment of the Anti-Locust Research Centre at the British Museum (Natural History) marks an important step in solving problems of locust control. One of the main functions of that organisation has been the assembling and recording of reports on the breeding and migrations of locusts in Africa and Western Asia. No fewer than 7,986 reports have been received from the Governments of the territories in these areas up to the end of 1945. The collation and sifting of the data thus acquired entails a large amount of detailed work, which is ultimately incorporated in the publications of the Anti-Locust Centre. These latter are planned in two series. First, memoirs of quarto size adapted for the publication of detailed charts, etc., devoted to biogeographical and bioclimatic papers; secondly, bulletins intended for the publication of papers on all other aspects of locust and grasshopper research and control. Up to date, two memoirs have appeared and a third is in the press. The first of the bulletins is also in the press.

Anti-Locust Memoir 1, by Z. Waloff, is entitled "Seasonal Breeding and Migrations of the Desert Locust (*Schistocerca gregaria*) in Eastern Africa" (1946; 76 pp., 30 maps)*. The primary purpose of this study was to analyse and describe the seasonal breeding and migrations of the swarms of this locust in the East African area. The material used to form the basis of this study was the data relating to an outbreak of this insect lasting from 1928 until 1931, and to the outbreak from August 1941 to February 1945. It appears that there is no inherent urge on the part of this locust to migrate in any particular direction or to search for suitable breeding grounds. The major trends of migrations are down the prevailing winds and change with them: old mature swarms, however, tend to fly against the wind. The distribution of the swarms in any season is largely dependent on the pattern of the air temperatures and winds. The incidence of breeding depends, among other factors, on the incidence of suitable rainfall conditions. Because of this, and of the mobility of swarms, the location of breeding areas is not constant but follows seasonal fluctuations of rainfall.

Anti-Locust Memoir 2 is by Miss V. Morant, and is entitled "Migrations and Breeding of the Red Locust (*Nomadacris septemfasciata*) in Africa, 1927–1945" (1947; 60 pp., 32 maps). The outbreak considered in this memoir lasted from 1927 until 1944, a period of more than eighteen years, during which time swarms were recorded from the Anglo-Egyptian Sudan and British Somaliland southwards to the Union of South Africa. In other words, the whole of Africa south of the equator was infested at some time or another during this outbreak, excepting certain coastal areas and the Equatorial Rain-Forest Belt in the north. The greater part of the material used in this study was derived from monthly reports sent to the Anti-Locust Centre from the various countries that were invaded during the outbreak. No fewer than 23,270 records of swarms have been received at this Centre, which enabled the application of cartographical methods to obtain a more complete picture of the rise and decline of the outbreak than has been previously available for any locust.

This same species of locust also forms the subject of an extensive paper by A. P. G. Michelmore in the *Bulletin of Entomological Research* (**37**, pt. 3, 331; 1947), and entitled "The Habits and Control of the Red Locust in Outbreak Areas and Elsewhere". The last great invasion of this insect started almost certainly from two restricted areas only, namely, the Mwera Marsh in the extreme north of Northern Rhodesia and Lake Rukwa in the south-west of Tanganyika Territory. The regular and constant observation of these areas is of prime importance, in that it enables incipient swarms to be destroyed, as happened in the rainy seasons of 1942–43 and 1943–44. At present, the best method of control in widespread campaigns is arsenical baiting. It is hoped, however, that insecticidal dusting from aeroplanes will soon be possible. The use of arsenicals puts certain limitations on campaigns on account of their danger to

* Copies available to institutions and persons engaged in locust and grasshopper research, in exchange for their publications. Requests to be addressed to the Director, Anti-Locust Research Centre, British Museum (Natural History), London, S.W.7. Also obtainable from "The Times" Printing Works, Richmond, Surrey. Memoir 1, 8*s.* post paid; Memoir 2. 6*s.* post paid.

man and stock, and the expense entailed owing to the need for close European or other reliable supervision. The author stresses the need for discovering less dangerous compounds both for terrestrial and aerial methods of control. He discusses the habits of the red locust in detail and stresses the importance of preventing outbreaks by controlling them at the source. The possibility of making these areas unsuitable for the species is also discussed. In this connexion draining, flooding and the prevention of grass fires are possible in some areas but not in others.

A. D. IMMS

FORTHCOMING EVENTS

*(Meeting marked with an asterisk * is open to the public)*

Monday, July 14—Thursday, July 17

CHEMICAL SOCIETY (in London).—Centenary Celebrations.

Monday, July 14

At the Science Museum, South Kensington, London, S.W.7.—Opening of the Centenary Exhibition by Prof. C. N. Hinshelwood, F.R.S.

Tuesday, July 15

At the Central Hall, Westminster, London, S.W.1.—Reception by the President and Council; Prof. C. N. Hinshelwood, F.R.S.: Centenary Address.

Wednesday, July 16

At the Royal Institution, Albemarle Street, London, W.1.—Prof. E. K. Rideal, F.R.S.: "The Work of the Royal Institution in Physical Chemistry in Great Britain".

At the Institution of Civil Engineers, Great George Street, London, S.W.1.—Prof. J. Read, F.R.S.: "Chemical Personalities a Century Ago".

At the Central Hall, Westminster, London, S.W.1.—Sir Robert Robinson, P.R.S.: The Faraday Lecture.

Monday, July 14—Saturday, July 19

SOUTH EASTERN UNION OF SCIENTIFIC SOCIETIES (in the Royal Pavilion, Brighton).—Fifty-first Annual Congress.

Tuesday, July 15

At 8 p.m.—Prof. W. A. F. Balfour-Browne: "The Possibilities of Natural History" (Presidential Address).

Thursday, July 17

At 8 p.m.—Film: "The Beginning of History", with Introductory Lecture by Dr. E. Cecil Curwen.*

Friday, July 18

At 10 a.m.—Discussion on "The Place of Scientific Societies in the Promotion of Science".

Thursday, July 17

BRITISH INSTITUTE OF RADIOLOGY (in the Reid-Knox Hall, 32 Welbeck Street, London, W.1), at 8 p.m.—Dr. John H. Lawrence (University of California): "The Application of Artificial Radioactivity to Biology and Medicine" (Twenty-fourth Mackenzie Davidson Memorial Lecture).

Thursday, July 17—Thursday, July 24

XITH INTERNATIONAL CONGRESS OF PURE AND APPLIED CHEMISTRY (in London).

Thursday, July 17

At 10.30 a.m. (at Central Hall, Westminster, London, S.W.1).—Opening Ceremony by Lord Leverhulme; at 2.30 p.m. (at the Imperial College of Science and Technology, South Kensington, London, S.W.7).—Dr. L. Pauling: Congress Lecture.

Friday, July 18

At 2.30 p.m. (at the Imperial College of Science and Technology, South Kensington, London, S.W.7).—Sir Henry Dale, O.M., F.R.S. Congress Lecture.

Tuesday, July 22

At 2.30 p.m. (at the Imperial College of Science and Technology, South Kensington, London, S.W.7).—Prof. L. Hackspill: Congress Lecture.

Thursday, July 24

At 10.30 a.m. (at Central Hall, Westminster, London, S.W.1).—Lecture by Sir Robert Robinson, P.R.S.

Friday, July 18—Saturday, July 19

INSTITUTE OF PHYSICS, INDUSTRIAL RADIOLOGY GROUP (at the Electric Lamp Manufacturers' Association, 2 Savoy Hill, London, W.C.2).—Symposium on "Methods of Crack Detection".

Friday, July 18

At 10 a.m.—Dr. W. Betteridge: Introductory Address; Papers on "Radiological Methods" and "Visual, Etching and Magnetic Methods".

Saturday, July 19

At 9.30 a.m.—Annual General Meeting of the Group; at 10 a.m.—Papers on "Eddy-current Methods" and "Crack Detection by Supersonic Methods".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER IN PHYSIOLOGY—The Dean, Medical College of St. Bartholomew's Hospital, West Smithfield, London, E.C.1 (July 18).

TEACHER OF BIOLOGY to Inter.B.Sc. standard at the Coventry Technical College—The Director of Education, Council House, Coventry (July 19).

ENGINEER IN THE AUDIO FREQUENCY SECTION of the Research Department based in London—The Engineering Establishment Officer, British Broadcasting Corporation, Broadcasting House, London, W.1 (July 19).

LECTURER IN MECHANICAL ENGINEERING—The Clerk to the Governors, Heanor Technical Institute, Heanor, Nottingham (July 19).

SECRETARY to the recently created Institute of Education—The Secretary and Registrar, The University, Bristol (July 20).

ZOOLOGIST or ENTOMOLOGIST (male) for studies on the fauna of forest soils in relation to fertility—The Secretary, Rothamsted Experimental Station, Harpenden, Herts. (July 26).

ASSISTANT LECTURER IN GEOLOGY—The Registrar, The University, Manchester 13 (July 26).

ASSISTANT LECTURER IN PURE MATHEMATICS—The Registrar, University College, Singleton Park, Swansea (July 26).

SENIOR ASSISTANT TEACHER IN THE MECHANICAL ENGINEERING DEPARTMENT—The Secretary, South-East London Technical Institute, Lewisham Way, London, S.E.4 (July 26).

SENIOR LECTURER IN ACCOUNTING in the University of the Witwatersrand, Johannesburg—The Secretary, Universities Bureau of the British Empire, 8 Park Street, London, W.1 (July 30).

SENIOR LECTURER IN ORGANIC CHEMISTRY, and a SENIOR LECTURER IN INORGANIC AND ANALYTICAL CHEMISTRY, in the Rhodes University College, Grahamstown—The Secretary, Office of the High Commissioner for the Union of South Africa, Trafalgar Square, London, W.C.2 (July 31).

LECTURER IN THE DEPARTMENT OF GEOLOGY—The Secretary, The University, Aberdeen (July 31).

LABORATORY TECHNICIAN IN THE DEPARTMENT OF PHYSIOLOGY—The Registrar, The University, Liverpool (August 1).

LABORATORY ASSISTANT IN THE PATHOLOGICAL UNIT at the Barking Hospital—The Town Clerk, Town Hall, Barking, Essex, endorsed 'Laboratory Assistant' (August 15).

SENIOR PRINCIPAL SCIENTIFIC OFFICER in the Ministry of Supply at the Chemical Research and Development Department, Waltham Abbey—The Secretary, Civil Service Commission, 6 Burlington Gardens, London, W.1, quoting No. 1937 (August 15).

SENIOR PRINCIPAL SCIENTIFIC OFFICER to take charge of research and development work on aircraft fire control equipment in the Armament Department of the Royal Aircraft Establishment, Farnborough—The Secretary, Civil Service Commission, 6 Burlington Gardens, London, W.1, quoting No. 1938 (August 15).

LECTURER IN ELECTRICAL ENGINEERING in the University of Cape Town—The Secretary, Universities Bureau of the British Empire, 8 Park Street, London, W.1 (August 21).

HEAD OF THE MATHEMATICS DEPARTMENT—The Principal, Royal Technical College, Salford 5 (August 23).

READERSHIP IN ANATOMY at St. Thomas's Hospital Medical School—The Academic Registrar, University of London, Senate House, London, W.C.1 (August 26).

RESEARCH STATISTICIAN, an ASSISTANT STATISTICIAN, and a MATHEMATICAL COMPUTER—The Secretary, Rothamsted Experimental Station, Harpenden, Herts.

LECTURER IN THE SCIENCE AND TECHNOLOGY OF REFRIGERATION to the standard of the City and Guilds syllabus—The Hon. Secretary, Institute of Refrigeration, Empire House, St. Martins-le-Grand, London, E.C.1.

ASSISTANT IN RESEARCH IN THE DEPARTMENT OF COLLOID SCIENCE—The Professor of Colloid Science, Free School Lane, Cambridge.

HEAD OF THE DEPARTMENT OF CHEMISTRY—The Principal, Sir John Cass Technical Institute, Jewry Street, London, E.C.3.

LECTURER IN BACTERIOLOGY—The Secretary, King's College of Household and Social Science, Campden Hill Road, London, W.8.

SENIOR MINING GEOLOGIST—The Secretary, Mianral, Teoranta, Four Provinces House, Harcourt Street, Dublin.

LECTURER IN IMPLEMENTS AND MACHINERY in the Faculty of Agriculture and Horticulture—The Registrar, The University, Reading.

PROFESSOR OF PHYSICAL METALLURGY—The Dean, Faculty of Applied Science, University of Toronto, Toronto, Ont., Canada.

LECTURER IN GEOGRAPHY in the University of Otago, Dunedin—The High Commissioner for New Zealand, 415 Strand, London, W.C.2.

LECTURER IN PHYSIOLOGY AND ZOOLOGY—The Registrar, Technical College, Sunderland.

SENIOR ASSISTANT, and a LECTURER, with special responsibility IN MECHANICAL AND PRODUCTION ENGINEERING, and ASSISTANTS with qualifications in Mathematics and Physics and/or Engineering Drawing and Engineering Science—The Principal, Technical College, Walsall.

SENIOR ASSISTANT IN ELECTRICAL ENGINEERING, specializing in Design of Electrical Machinery, a LECTURER IN MECHANICAL ENGINEERING to Degree and Higher National Certificate students, and a LECTURER IN MATHEMATICS mainly to National Certificate students—The Principal, College of Technology and Arts, Rugby.

PROFESSOR OF CHEMISTRY, a PROFESSOR OF BOTANY, a PROFESSOR OF ZOOLOGY, and a SENIOR LECTURER IN PHYSICS, in the University College of the West Indies—The Secretary, Inter-University Council for Higher Education in the Colonies, 8 Park Street, London, W.1.